SOCIAL ATTENTION IN YOUNG TYPICALLY DEVELOPING AND AT-RISK CHILDREN: EYE TRACKING PARADIGMS AND IMPLICATIONS FOR UNDERSTANDING DEVELOPMENTAL TRAJECTORIES

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ABSTRACT

The adaptive trait of perceiving and apportioning eye movements and gaze behaviors forms one of the basic foundations of social cognition in infants. Thus, diminished eye gaze in individuals is known to be an early behavioral risk marker for autism spectrum disorders (ASD). Research studies in ASD have shown numerous advances; however, the field still lacks a systematic approach for integrating the behavioral and biological markers that can be used in community settings for better identification, timely access to diagnosis, and the implementation of evidence-based interventions. The aim of the first two papers was to analyze the longitudinal gaze behaviors of young infants and toddlers during an eye-tracking paradigm and the relations to joint attention and language development skills. The aim of the third paper was to classify any disparities in the age of ASD diagnosis. Together, this dissertation study examined the red flags associated with gaze behaviors and the age at ASD diagnosis in order to inform early identification and diagnostic practices for ASD. In addition, methodological techniques for examining longitudinal gaze patterns during the early years of development are discussed. These investigations further demonstrate the importance of early identification of ASD for infant siblings of children with ASD, highlighting the heterogeneous symptomology and diagnostic challenges associated with the disorder. Improved efforts toward earlier identification will allow practitioners to tailor intervention services that provide the most optimal results for individuals with ASD. Overall, the study contributes empirical knowledge regarding typically developing and infants at-risk's preferences for social attention, with direct implications for endophenotypic markers for young children with ASD. Furthermore, despite the increased awareness of ASD, the child's age at first ASD diagnosis remains delayed, resulting in a need for inquiry of the disparities that may exist due to individual and sociodemographic factors.

CHAPTER I: INTRODUCTION

Human beings have exceptional social and cognitive abilities in contrast to other mammals (Carpenter et al., 1998; Davis & Carter, 2014). This adaptive trait to perceive, recognize, and influence the behaviors of others forms the basic foundation of social cognition and intelligence in infants (Aslin, 2007; Senju & Csibra, 2008). When these skills are disrupted in very young children, it is considered to be a risk factor for autism spectrum disorders (Klin, Shultz, & Jones, 2015; Tager-Flusberg, 2010). Autism spectrum disorders (ASD) is characterized by restricted, repetitive interests and deficits in social interaction and communication (Barbaro & Dissanayake, 2009; Lord & Jones, 2012; Zwaigenbaum, Bryson, & Garon, 2013). Currently, ASD, a neurodevelopmental disorder, occurs in 1 out of 68 children and stands among the most prevalent of the childhood neuropsychiatric disorders (Centers for Disease Control and Prevention, 2016; Fakhoury, 2015; McPartland et al., 2012). Despite known genetic and neurobiological underpinnings, ASD currently lacks clear biological markers; consequently, clinicians tend to rely exclusively on observable and behavioral symptoms for diagnoses (Elsabbagh et al., 2012; Zwaigenbaum et al., 2015b).

Although heterogeneous in causes and presentation, ASD has an early onset, with at risk signs typically first appearing around 12 to 18 months (Barbaro & Halder, 2016; Zwaigenbaum et al., 2015a). However, despite significant progress seen in screening and surveillance, one of the greatest challenges remains in the early detection of ASD, and many children remain undiagnosed until approximately age four or five (Daniels & Mandell, 2013; Lord & Jones, 2012). Early recognition of ASD-related risk behaviors and timely interventions can have cascading effects across adaptive, cognitive, and developmental domains (Barbaro & Halder, 2016; McMorris et al., 2013; Zwaigenbaum et al., 2013). Specifically, by examining longitudinal

trajectories of eye gaze patterns during infancy, this dissertation study adds to preliminary evidence of initial developmental differences in children at-risk for or with ASD, particularly as related to social attention, language, and joint attention (Barbaro & Halder, 2016; Emerson, Morrell, & Neece, 2015; Falck-Ytter, Bölte, & Gredebäck, 2013). Additionally, through a person-centered approach, subgroups of children with ASD are identified based on common classes of sociodemographic factors associated with diagnostic delays. This evidence may serve to reduce time to diagnosis for vulnerable populations leading to timelier interventions (Daniels & Mandell, 2013; Lord & Jones, 2012). Thus, this dissertation study examined: (1) the developmental trajectories associated with typically developing (TD) infants' eye gaze patterns during dynamic visual scenes; (2) the risk behaviors in social attention in infants classified to be at-risk for ASD; and (3) a person-centered approach to highlight heterogeneity and diagnostic delays across a population of 8-year-old children with ASD.

Background

Navigating a complex environment with behaviors such as orienting to name and gaze following requires infants to flexibly allocate eye gaze to obtain socially relevant information (Carlin & Calder, 2013; Elison et al., 2013). Of particular importance in developmental trajectories is the infant's ability to process information about others' eye gaze and joint attention behaviors. These early social behaviors support an understanding of emotional states, language development, social and joint attention, imitative learning, and goal-directed acts (Falck-Ytter et al., 2013; Theuring, Gredebäck, & Hauf, 2007). Specifically, joint attention refers to considering one's own visual attention in conjunction with that of others in order to jointly reference and exchange meaningful information (Jones & Carr, 2004; Mundy, Sullivan, & Mastergeorge, 2009; Tomasello, 1995). One expedient way to understand the development and distribution of gaze in

young children is to record their eye movements. A driving factor behind recording overt eye movements is that one's gaze provides evidence of visualization patterns and social intelligence during key developmental periods (Aslin & McMurray, 2004; Duchowski, 2007; Elsabbagh & Johnson, 2016).

In general, eye gaze provides both a unique developmental guide to joint visual attention and a mechanism for understanding the goals, intentions, and mental states of others (Gredebäck, Theuring, Hauf, & Kenward, 2008; Theuring et al., 2007; Ristic et al., 2005). However, reduced eye contact and decreased joint attention are among the hallmark deficits in young children at risk for or diagnosed with ASD (Fakhoury, 2015; Jones & Klin, 2013; Mercadante, Macedo, Baptista, Paula, & Schwartzman, 2006). To understand the significance of early identification and intervention for young children, it is critical to characterize the ASD phenotype in the first two years (Frank, Amso, & Johnson, 2014; Rogers, 2009; Zwaigenbaum et al., 2015b). That is, risk behaviors as depicted through eye gaze patterns provide a potential endophenotypic mechanism for understanding the ASD pathogenesis (Klin et al., 2015). Consequently, eye-tracking technology may be ideally suited for examining atypical behaviors associated with social attention in ASD, specifically in very young children (Gredebäck, Johnson, & von Hofsten, 2009; Pierce et al., 2015). A major advantage of the eye tracker is its ability to non-invasively capture dynamically complex phenomena with accurate spatial and temporal resolutions. Furthermore, the eye tracker is especially suited for infants, as it does not require verbal affirmations or advanced motor responses (Aslin & McMurray, 2004; Holmqvist et al., 2011; Horsley, 2014).

By employing eye-tracking paradigms and capturing TD and at-risk infants' gaze trajectories, professionals can identify factors that impact social attention. These developmental

trajectories can be compared to detect deviating patterns and ASD symptom-emergence for improved measures of identification, diagnosis, and positive interventions (Rogers, 2009; Zwaigenbaum et al., 2015a). Decades of research have reported the importance of following another's gaze for the optimal development of social attention and communication (Scaife & Bruner, 1975; Tomasello, 1995). From early development, infants display preferential attention towards social stimuli such as eye gaze and faces (Elsabbagh et al., 2013a; Jones, Carr, & Klin, 2008). For instance, at approximately one month, infants begin to scan the edges of human faces such as the hairline and chin. Close to two months, infants focus on the eyes and mouth more than any other facial features (Leekam, Hunnisett, & Moore, 1998; Pierce, Muller, Ambrose, Allen, & Courchesne, 2001). Furthermore, from eight weeks, infants are able to smile in response to eye contact, and by nine weeks, infants fixate on an adult's eyes (Beier & Spelke, 2012; Haith, Bergman, & Moore, 1977). Between six and 26 weeks, infants' scanning progresses to adult-like patterns that stabilize around 18 weeks (Hayhoe, 2004; Hunnius & Geuze, 2004). In sum, these social attention behaviors allow infants to obtain and predict information about external and internal events such as linguistic information, emotional cues and regulation, and goal-directed actions (Sterling et al., 2008; Webb, Dawson, Bernier, & Panagiotides, 2006).

Conversely, eye gaze behaviors seem to be disrupted in individuals with ASD, suggesting cascading effects related to reduced social attention (Chita-Tegmark, 2016a; Chawarska, Macari, & Shic, 2013). One of the goals of eye-tracking with genetically linked at-risk infants (i.e. infant siblings of children diagnosed with ASD) is to discover reliable biomarkers that accurately identify individuals with ASD (Ames & Fletcher-Watson, 2010; Pierce et al., 2015; Zwaigenbaum et al., 2009). For instance, through eye-tracking paradigms, researchers have correlated reduced attention to social stimuli and increased attention to non-social stimuli with

behavioral measures of autism (Chita-Tegmark, 2016b; Guillon et al., 2014; Papagiannopoulou et al., 2014). Furthermore, studies focused on language development and facial processing, such as gaze towards the speaker's eyes and mouth, have also been significantly correlated with behavioral assessments of social attention (Parish-Morris et al., 2013; Young et al., 2009). Despite these social deficits being hallmarks of ASD, uncertainty remains as to whether attention to social and non-social stimuli is fundamentally reduced or nonexistent in individuals with ASD (Chita-Tegmark, 2016a; Klin et al., 2002; Papagiannopoulou et al., 2014; Shic et al., 2012). The field of eye-tracking research with at-risk infant populations benefits from analytic techniques that capture the overt "red-flags" associated with ASD.

Despite the methodological strengths of eye tracking paradigms producing extensive eye gaze data, only a handful of studies have used dynamic social stimuli to prospectively examine infants' visual attention. Although many studies have demonstrated differences in behavioral and neurobiological eye gaze behaviors (e.g., Akechi et al., 2011; Pelphrey et al., 2002; Senju & Csibra, 2008), we still know little about the development of social attention in infants outside of static stimuli. For example, many studies have only measured infants retrospectively or at specific ages after obtaining an ASD diagnosis, without observing prospective trajectories of social attention (Boraston & Blakemore, 2007; Tager-Flusberg, 2010). Furthermore, understanding the onset or decline of atypical gaze behaviors in a novel paradigm may be crucial for underlining patterns that occur within a high-risk population (Jones & Klin, 2013; Merin et al., 2007; Taylor & Herbert, 2013).

A prospective investigation of early risk markers identifies behaviors that are analogues to later occurring autism and determines how these behaviors may reduce the child's social and cognitive learning opportunities (Ames & Fletcher-Watson, 2010; Zwaigenbaum et al., 2005).

Despite retrospective parental reports and prospective infant sibling research indicating ASD "red flags" as early as 12 months, there is a significant delay between initial concerns and formal diagnoses, which usually occur around age four or five (Barbaro & Dissanayake, 2009; Barton et al., 2012; Daniels & Mandell, 2013; Lord & Jones, 2012). This "diagnostic odyssey" of approximately two years reflects a critical need to identify reliable markers across infancy. However, the heterogeneity of ASD requires careful consideration of the methods used to determine behavioral risk factors. Because abnormal neural systems have been identified within ASD populations, eye gaze behaviors can be quantified during the critical period of infancy when intervention is considered to be most effective (Pierce et al., 2015; Zwaigenbaum et al., 2013). In addition, it is specifically through our understanding of typical gaze patterns that gaze deviations and reduced social attention can be accurately compared and detected prior to the onset of ASD (Fakhoury, 2015; Falck-Ytter et al., 2013).

In conjunction with the detection of atypical eye gaze patterns in ASD, risk factors at the familial and environmental level such as race, geographic location, socioeconomic status, paternal age, and others need to be additionally characterized (Emerson et al., 2015; Koegel et al., 2014; Mandel et al., 2005). That is, rather than looking at individual independent variables, a person-centered approach allows for a collective investigation of interrelated factors that can be attributed for the delayed detection rates for ASD. Some of these known independent factors include provider biases, lack of knowledge for ASD "red flags", culture, and other structural and organizational factors (Daniels & Mandell, 2013; Emerson et al., 2015; Shattuck et al., 2009). Subsequently, this approach can help clinicians understand the clinical onset and adopt optimal practices when working with individuals with ASD (Rogers 2009; Zwaigenbaum et al., 2009). By investigating and identifying the collective risks associated with delays in ASD diagnosis,

researchers can reduce gaps between early identification and diagnosis. Considering that ASD is usually not diagnosed until approximately the age of four in most children, work on identifying the early atypicalities remains a priority in ASD research (Daniels & Mandel, 2013; Emerson et al., 2015).

Dissertation study outline

This dissertation is comprised of three manuscripts and one of the primary aims of this dissertation was to describe the eye gaze patterns in infants and toddlers considered to be typically developing and at-risk for ASD. Using exploratory analyses, gaze behaviors were captured during dynamic social scenes to investigate atypical patterns related to social attention. A second aim of this dissertation was to identify through a person-centered approach collective classes of individual and sociodemographic factors associated with ASD diagnostic delays. This study conceptualized risk factors as unique constellations of various interactional behaviors such as race, severity of ASD, functionality, which as opposed to descriptions of individual behaviors, comprise the global risk context for ASD diagnosis. More specifically, I examined the following research questions, each corresponding to the aims of the individual manuscripts:

1) What eye gaze patterns (gaze durations) are associated with the first two years of typical human development?
2) What eye gaze patterns (gaze durations) are associated with infants and toddlers considered at-risk for ASD during the first two years of development?
3) Among children diagnosed with ASD, can we identify subgroups that are more at risk for delayed diagnoses?

Through the examination of these research questions, this study capitalizes on the readily observable and quantifiable gaze behaviors within the context of social attention during infancy.

Furthermore, the study has implications for assessing developmental trajectories for the purposes of early identification and diagnosis of ASD.

Paper #1: Visual social attention in typically developing infants and toddlers: a longitudinal examination of gaze patterns

Over the course of the first year, an infant processes others' gaze in order to make inferences about emotions, goals, attention, and communicative signals (Scaife & Bruner, 1975; Senju & Csibra, 2008; Wagner, Luyster, Yim, Tager-Flusberg, & Nelson, 2013). Despite the widespread studies on individuals' gaze following and gaze behaviors, there is a paucity of research involving infants and their gaze patterns during dynamic stimuli. The present study seeks to fill that gap by examining the eye gaze patterns of TD infants and toddlers across four key developmental time points (i.e. between the ages of 3-24 months). The goals of this paper included describing longitudinal eye gaze patterns depicted during the presentation of dynamic social scenes of *The Muppets Movie*. In addition, these patterns of social attention were compared with measures of adaptive behaviors and social development skills such as language and joint attention.

Paper # 2: Visual social attention in at-risk infants and toddlers: a longitudinal examination of gaze patterns

With many prospective studies taking place with high-risk infants, the investigator's focus should remain on identifying early risk factors and translating them to applied settings for active surveillance and screening (Bryson et al., 2007; Zwaigenbaum, Bauman, Stone, et al., 2015). The investigation of early risk indicators and phenotypic markers using eye-tracking technology can serve to be a powerful clinical resource for early detection of ASD, especially for a population that can greatly benefit from early identification and intervention (Kasari, Gulsrud,

Wong, Kwon, & Locke, 2010; Rogers et al., 2012; Zwaigenbaum, Bauman, Choueiri, Kasari, et al., 2015). Thus, the second paper analyzed the longitudinal eye gaze patterns of infants and toddlers classified as at-risk, including infant siblings of children diagnosed with autism. The eye gaze patterns were assessed across four time points between the ages of three to 30 months. The same analytic tools from paper one were retained for the current study in order to describe the longitudinal gaze patterns during dynamic audio and visual scenes. Additionally, the relationship between these patterns and measures of developmental outcomes including language, joint attention, and adaptive behavior skills were explored. A major aim of this paper was to identify and explicate the ways in which eye gaze patterns as related to social attention in these groups differed from those of TD peers.

Paper # 3: Characterizing health disparities in the age of autism diagnosis among 8-yer-old children

Through the investigation of early developmental trajectories of infant siblings who have a higher recurrence risk for ASD, considerable individual, familial, and societal costs related to ASD can be addressed early on through timely intervention services (Matson, Wilkins, & González, 2008; Zwaigenbaum, Bauman, Stone, et al., 2015). These sibling investigations have yielded critical insights not only on the early symptomology, but also on the time course to an ASD diagnosis. The final paper in this dissertation study utilized a person-centered approach to examine the health disparities that may be contributing to the delays in the age of ASD diagnosis. Specifically, the identification of a subpopulation or groups of homogeneous classes that were indicated by sociodemographic and individual factors as well as condition severity were explored. Subsequently, these factors were linked with delays in the age of ASD diagnosis in order to better understand the health disparities that may be occurring for 8-year-old children

with ASD and their families. Through the identification of these classes of different demographic and socioeconomic barriers across a heterogeneous sample of children with ASD, diagnostic disparities and delays were investigated.

Summary

Collectively, these three papers describe the ASD-related early identification and early diagnostic processes through mechanisms of gaze trajectories and exploration of sociodemographic and individual factors related to symptom onset. The current research investigations will highlight the potential for utilizing eye-tracking paradigms with a highly accessible high-risk infant population group that has not been studied extensively. More specifically, the use of eye-tracking tools serves as a mechanism to further our understanding of visual social attention and the associated underlying atypical profiles that may assist investigators with evidence to inform targeted interventions for young children with developmental risk (Elsabbagh & Johnson, 2010; Zwaigenbaum et al., 2009). Furthermore, the evidence from the three individual papers is discussed in terms of future research related to social attention, early identification, and early intervention processes. The implications for clinical and diagnostic practices are discussed.

Chapter II: VISUAL SOCIAL ATTENTION IN TYPICALLY DEVELOPING INFANTS AND TODDLERS: A LONGITUDINAL EXAMINATION OF GAZE PATTERNS

Studies of eye gaze behaviors and social attention processing have conveyed the importance of tracking infants' abilities to attend to and interpret others' social behaviors (Akechi, Kikuchi, Tojo, Osanai, & Hasegawa, 2013; Beier & Spelke, 2012; Scaife & Bruner, 1975). Eye gaze behaviors and concomitant perceptual development serve as building blocks for navigating the social world and understanding the internal states of others (Beier & Spelke, 2012; Carlin & Calder, 2013; Farroni, Csibra, Simion, & Johnson, 2002; Tomasello, 1995). Adults regularly direct infants' attention toward the most salient information in the environment through mechanisms of gaze and ostensive cues such as pointing, gesturing, and language (Barry, Graf Estes, & Rivera, 2015; Senju & Csibra, 2008). Specifically, gaze behaviors such as mutual gaze, or gaze where two individuals are looking at each other, averted gaze where a person's attention is directed toward another person or object in the environment, and gaze following, which is the detection of shifted gaze resulting in an individual's directional motion to outside events, all serve to provide repeated learning opportunities for social understanding and engagement (Brooks & Meltzoff, 2005; Pfeiffer, Vogeley, & Schilbach, 2013). It is through this joint visual attention that infants learn to direct and coordinate attention between self, other, and the surrounding environment (Beier & Spelke, 2012; Carpenter & Nagell, 1998; Grossmann & Johnson, 2010; Jones & Carr, 2004; Pfeiffer et al., 2013; Tomasello, 1995). Joint attention plays a pivotal role in language learning through gestural cues and gaze behaviors that assist infants with mapping the words associated with events, people, and objects (Baldwin, Moore, & Dunham, 1995; Mundy & Gomes, 1998; Redcay, Kleiner, & Saxe, 2012).

Advancing our understanding of these early gaze behaviors requires applying emerging analytic techniques to capture infants' overt gaze in ecologically valid paradigms (Ahtola et al., 2014; Chevallier et al., 2015; Pfeiffer et al., 2013). Thus, the use of eye-tracking in comparison to traditional third-person observations proves to be advantageous for documenting infants' spontaneous processing of information (Duchowski, 2007; Gredebäck, Johnson, & von Hofsten, 2009). Only a few studies have examined infants' capabilities of detecting faces within complex dynamic stimuli outside of static experimental conditions (e.g. Di Giorgio, Turati, Altoè, & Simion, 2012; Frank, Vul, & Johnson, 2009; Guellai & Streri, 2011; Parise, Handl, & Striano, 2010). Therefore, one of the main goals of the current study is to apply an eye-tracking paradigm with dynamic stimuli in a longitudinal study of infants and toddlers to understand eye gaze behaviors and the concurrent joint attention and language skills. The term 'dynamic' is defined here as a stimulus that includes videos of individuals interacting together (moving their eyes towards and away, chewing, smiling, nodding, etc.) and incorporates continuous transient changes in facial expressions and movements.

The Development of Gaze Behaviors in Infants

In order to navigate the complexities of the social environment, infants learn to allocate gaze and visual attention to biologically relevant information (Carlin & Calder, 2013; Elison et al., 2013; Scaife & Bruner, 1975). Eye gaze behaviors are an essential advancement in infants' early development of social attention and communication. In general, eye gaze studies have indicated that infants have remarkable preferential attention for others' eye contact and responding to their own name (Grossmann & Johnson, 2010; Senju & Csibra, 2008), such that even postnatally infants demonstrate preferences for direct versus averted eye gaze (Bertenthal &

Boyer, 2015; Di Giorgio et al., 2016; Farroni et al., 2002; Tenenbaum, Shah, Sobel, Malle, & Morgan, 2013).

Several studies have described the development of eye gaze behaviors as *the* key mechanism to support subsequent acquisition of social cognition abilities (e.g., Beier & Spelke, 2012; Haith, Bergman, & Moore, 1977; Senju & Csibra, 2008; von Hofsten, Dahlström, & Fredriksson, 2005). These eye gaze behaviors allow infants to develop novelty preferences for salient events such as gaze orienting, human faces, and emotions (Akechi et al., 2013; Beier & Spelke, 2012; Gredebäck, Fikke, & Melinder, 2010). Among the first few studies to employ dynamic stimuli with eye-tracking, Hunnius and Geuze (2004) assessed ten infants' scanning patterns for a moving face versus an abstract stimulus. They reported that at the age of 14 weeks, the stimulus of the mother's face elicited more fixations than the abstract stimulus. Moreover, the overall time spent looking at the stimulus declined with age, but the number of fixations increased most rapidly between six and 18 weeks of age, indicating more advanced scanning skills by older infants (Hunnius & Geuze, 2004). Despite these reported eye gaze behaviors in very young children, what is less known is how infants and toddlers allocate attention across segments of the faces, especially when the faces are embedded within heterogeneous stimuli.

Gaze behaviors towards faces. Numerous studies have examined that despite a weak visual motor system, TD newborns show increased preferential attention to human faces (Turati, Simion, Milani, & Umiltà, 2002; Valenza, Simion, Cassia, & Umiltà, 1996; Walton, Bower, & Bower, 1992). For example, in a study with 24 newborn infants, Guellai and Streri (2011) found that through a familiarization-test procedure of unfamiliar talking faces that have either direct or averted gaze, newborns preferred looking longer at the face talking to them, but only when simultaneous direct gaze was involved. This study further supports the notion that eye gaze

modulates face recognition soon after birth (Farroni et al., 2002; Guellai & Streri, 2011; Haxby, Hoffman, & Gobbini, 2002). Additional studies on infants' face scanning patterns have revealed that across development, infants begin to focus more on the internal features of the face such as eyes and mouth (Easterbrook, Kisilevsky, Muir, & Laplante, 1999; Haith et al., 1977; Hunnius & Geuze, 2004; Leppänen, 2016). Having this biased orientation for the basic geometric form of faces early on, infants continue to develop robust skills over the course of the first year that allow them to become highly proficient at processing faces (Frank, Amso, & Johnson, 2014; Frank et al., 2009; Xiao et al., 2015).

The dynamic growth of preferential eye gaze toward faces and face-like patterns exemplifies the developmental trajectory necessary for advanced social perception in infants (Frank et al., 2009; Nele, Ellen, Petra, & Herbert, 2015). For instance, infants' ability to scan preferentially to the eyes first occurs around two months of age, with a gradual increase in facial recognition performance (Katarzyna Chawarska, Klin, & Volkmar, 2003; Haith et al., 1977; Taylor, Batty, & Itier, 2004). At approximately four months of age, infants are better at processing upright versus inverted faces, with eye contact further enhancing face recognition (Beier & Spelke, 2012; Jones, Carr, & Klin, 2008; Senju & Csibra, 2008; Webb et al., 2006). By six months, faces continue to attract infants' attention despite competing stimuli in their visual environments (Chawarska, Macari, & Shic, 2013; Gluckman & Johnson, 2013; Haith et al., 1977). Gliga et al., (2009) showed that faces captured a majority of six-month-old infants' attention among a variety of competing distracting images. Furthermore, these infants had greater first looks than expected by chance toward upright and inverted faces in comparison to the objects in the distractor category. Alongside facial recognition skills, it is also crucial to understand how an infant processes and prioritizes incoming social cues through the

development of gaze behaviors to specific parts of the stimulus (Beier & Spelke, 2012; Carlin & Calder, 2013). More specifically, infants show more biased looking towards human faces than less relevant stimuli such as stationary objects (Beier & Spelke, 2012; Valenza et al., 2015). For instance, the tendency for infants to maintain their attention to faces upon presentation of distracting stimuli increases significantly between five and seven months. Additionally, their attention becomes more selective over time such that faces with more complex, novel, and informative cues are preferred (Leppänen, 2016; Valenza et al., 2015). This narrowly tuned preference for faces within complex scenes becomes more reliable during the latter half of the infant's first year of life (Bertenthal & Boyer, 2015; Leppänen, 2016). Such corroborating evidence highlights the importance of an early preference for prototypical faces in infants that is pivotal for social learning (Gliga, Elsabbagh, Andravizou, & Johnson, 2009).

Gaze behaviors and joint attention. Eye gaze appears to provide unique developmental guidance for setting the foundation for the initiation of joint attention, as well as providing a mechanism for understanding the goals, intentions, and mental states of others (Brooks & Meltzoff, 2005; Mundy et al., 2007; Scaife & Bruner, 1975). An infant's capacity to use an adult's eye gaze as a social cue to attention (i.e. joint attention) develops early in life. The ability to utilize and follow another person's gaze direction is reliably established by 10-12 months of age (Gredebäck et al., 2010; Leekam & Hunnisett, 1998; Theuring, Gredebäck, & Hauf, 2007; von Hofsten et al., 2005). This attentional gaze behavior is further influenced by the child's simultaneous ability to attend to objects in the environment as well as the human cues that make these objects salient (Leekam & Hunnisett, 1998). This form of joint visual engagement gives rise to complex behaviors in infancy. More specifically, joint attention provides foundational building blocks for social cognitive development and language learning beginning in infancy

(Redcay et al., 2012; Sullivan, L., Mundy, P., & Mastergeorge, 2015; Tomasello, 1995). In the first year of development, infants learn to integrate the incoming stimuli from the environment that enable them to coordinate their visual attention with the social attention of others (Grossmann & Johnson, 2010; Mundy, Sullivan, & Mastergeorge, 2009; Redcay et al., 2012).

Empirical studies on joint attention suggest that infants' abilities to share a common reference point develops before spoken language (e.g., (Brooks & Meltzoff, 2005; Grossmann & Johnson, 2010; Swanson & Siller, 2013), thus serving as an important precursor to higher-level states and attributions such as theory of mind and goal-oriented thinking (Mundy et al., 2007; Vaughan Van Hecke et al., 2012). Understanding gaze behaviors and flexibly using others' gaze to orient attention towards the surrounding environment becomes an integral part of social perception (Frischen, Bayliss, & Tipper, 2007). For example, by orienting towards the object, an infant might have faster word recognition and acquisition of nouns through the pairing of the oriented gaze and the vocalized name (Baron-Cohen, 1995; Brooks & Meltzoff, 2005). Thus, gaze behaviors, especially within the social context of gaze cueing and face perception, can provide building blocks of joint attention and language skills.

Gaze behaviors and language processing. Studies on the subtleties of facial processing have revealed that the eyes and mouth may differentially attract the gaze interest of infants (Farroni, Johnson, & Csibra, 2004; Young, Merin, Rogers, & Ozonoff, 2009). An eye-tracking study conducted by Wagner and colleagues (2013) with 117 infants found that infants displayed more attention to the core features of the face such as the eyes, as assessed by overall duration and proportion of time spent viewing their mother's versus a stranger's face. Furthermore, in comparison to six- and nine-month-olds, 12-month-olds showed decreased attention to the eyes and increased attention to the mouth (Wagner et al., 2013). This preferential tracking of the eyes

relative to the mouth has been suggested to be reflective of socio-emotional cues and language acquisition skills (Guillon, Hadjikhani, Baduel, & Rogé, 2014; Wagner et al., 2013).

Similarly, Lewkowicz & Hansen-Tift (2012) studied 179 four-, six-, eight-, 10-, and 12-month-old infants as they saw and heard a female speaking in the infants' native and non-native language. The authors concluded that regardless of language, between four and eight months of age, infants shifted their attention from decreased looking at the eyes to increased looking at the mouth. Another shift occurred as 12-month-olds began shifting their attention back toward the eyes in response to native but not non-native language. These gaze shifting patterns were attributed to the infant's growing acquisition of speech perception, developing expertise in their native language, and speech production abilities during this developmental period (see Bahrick & Lickliter, 2000; Streri, Coulon, & Guellaï, 2012; Young et al., 2009). More specifically, studies have found that after six months of age, infants are able to match faces with voices based on age, gender, and expressions as a result of complex hierarchical intersensory relations such as incoming auditory and visual spatial cues (Bahrick, Netto, & Hernandez-Keif, 2008; Gogate & Bahrick, 1998; Walker-Andrews, Bahrick, Raglioni, & Diaz, 1991). For example, the temporal synchrony between the rhythms, the nature of speech sounds, a moving mouth, and gaze behaviors allow the infant to process concurrent presentation of the same information coming from multiple sense modalities (Bahrick & Lickliter, 2000). This intersensory integration of faces and voices allows the infants to further differentiate the multisensory experiences necessary for language acquisition and advancement (Bahrick & Lickliter, 2000; Hillairet de Boisferon, Tift, Minar, & Lewkowicz, 2016; Patterson & Werker, 2003; Streri, Coulon, Marie, & Yeung, 2016). In sum, the ability to follow eye gaze and focus greater attention to the speaker's mouth across infancy can influence the infant's acquisition of language (Lewkowicz & Hansen-Tift,

2012; Morales et al., 2000; Tenenbaum et al., 2013). Therefore, the relations between attention to the eyes and the attention toward the mouth are indicative of and crucial for the development of social and language skills.

Present Study

The evidence on infant's increased attention to faces with direct and averted gaze is congruent across many reported studies (Farroni et al., 2002; Guellai & Streri, 2011); however, what is less known is how the infant orients and sustains attention toward faces during the presentation of dynamic stimuli (Di Giorgio et al., 2012; Gliga et al., 2009). Through the investigation of infants' early eye gaze patterns and attentional preferences towards faces in ecologically valid designs, researchers can understand the trajectories of typical gaze behaviors with precision. However, research employing dynamic eye-tracking paradigms for infants' gaze patterns has been scarce with most studies focused on static stimuli to assess changes in saccades, attentional control, and face recognition. This is of interest because visual attention in young infants predicts the subsequent trajectories of social attention and cognition (Frank et al., 2009; Scaife & Bruner, 1975). The present study is guided by three central research questions:

(1) What are the longitudinal eye gaze trajectories of TD infants and toddlers during dynamic social scenes from three to 24 months of age?

(2) What regions of the stimuli do infants focus on and how does this change with age?

(3) How do these eye gaze patterns relate to developmental measures of joint attention, language development, and adaptive behaviors?

I hypothesized that infants and toddlers overall would display longer fixation durations for human faces despite distracting stimuli such as objects and the background. In addition, with age, infants and toddlers would display longer fixation durations for the mouth than the eyes, as

the mouth would provide more support for pre-verbal cues and language development (Parish-Morris et al., 2013; Young et al., 2009). And, that there would be positive associations between eye gaze trajectories, joint attention, and early language development.

Methods

Sample. Data for this study were drawn from the longitudinal Interactive Eye Gaze study (IEGS). The IEGS collected data from the larger Tucson area during the years 2013-2017. The inclusionary criteria for the TD infants were full-term births without any complications and no known developmental delays according to parental reports. The TD participants included 73 infants at visit one from English speaking homes who were recruited between the ages of three to 24 months (M = 9.44, SD = 5.19). A total of 41 males and 32 females participated in the study at visit one. For participants who contributed to longitudinal data for a total of four time points (i.e. four visits separated by three months each), the total sample included N = 30. Table 1 displays the demographic information for this sample across the four assessed time points.

Procedure. Informed written consent was obtained from the parents during the initial visit to the lab. Families followed the same procedure for all four visits. All infants participated in a series of standardized developmental assessments by an examiner in order to understand the developmental profiles of these participants (see measures sections below). In addition, parents completed standardized questionnaires regarding their children's adaptive behaviors and language development. Next, the infants were placed in an adjustable high-chair in front of the eye-tracking computer along with their mothers seated next to them, but facing away from the tracker for the presentation of the dynamic stimulus. Each participant's session lasted approximately 90 minutes.

Apparatus and Eye-tracking Paradigm. The Tobii Studio (T60; Tobii Technology, Sweden) eye-tracking model was utilized for this study. This eye-tracking software employs near infrared illumination in order to create the reflection patterns on the cornea and pupil of the eyes of the participant. Advanced image processing algorithms are used to estimate the accurate position of the eye in space and the point of gaze. The T60 eye-tracking model captures data rates at 60 HZ from a 17-inch TFT monitor, situated 65 cm away from the infant. This eye-tracking model allows for a large degree of head movement, with an accuracy of 0.5-1 degree of visual angle. In the current study, scenes from the 1979 version of *The Muppets Movie* (two minutes and 10 seconds) were chosen. The video clip was presented on a 1280 by 1024 pixels screen resolution with built in speakers for audio control. The audio was the original soundtrack from the movie. *The Muppets Movie* depicted a frog (Kermit), a pig (Ms. Piggy), and an adult male (Server) engaged in conversation during dinner. Frames from this stimulus are shown in Figure 1. The dynamic clip featured actors' mutual gaze, averted gaze, and movements towards and away from the camera. The stimulus contained light music in the background that was overlapped by the actors' dialogues in English. The actors spoke approximately the same amount of time with brief silent period in between transitions. This stimulus was chosen primarily because it provided rich visual experiences as well as a range of facial expressions and triadic social interactions.

Eye-Tracking Calibration. While seated in the infant/toddler chair or on the mother's lap, a five-point calibration system was used to establish the individualized eye movements of each infant. The calibration process involved a looming/vanishing blue circle presented on a background of white dots, at each corner of the screen and in the center. At each location, calibration data was collected after consistently hearing three beeping sounds ("dings"). After the

calibration process, the researcher examined a plot of gaze data recorded during the acquisition of each calibration point, eliminating any data points where the infant and toddler was not looking at the target. If enough calibration data was not collected the first time, the infants underwent the same process again.

Measures. *Demographic Information*. Basic demographic information was collected in order to gather information for both the child's and the parent's age, as well as the parent's education, race, and marital status (see Table 1).

The Early Social-Communication Scales (ESCS). The ESCS (Mundy, P., Delgado, C., Block, J., Venezia, M., Hogan, A., & Seibert, 2003) is a filmed 15-20 minutes structured observation between the examiner and the child engaged in play. The ESCS observes nonverbal communication in children eight to 30 months of age. The filmed observations were classified by coders into one of three mutually exclusive categories of early social-communication behaviors: Joint Attention Behaviors, Behavioral Requests, and Social Interaction Behaviors. Two independent coders watched all the video recordings of the ESCS in order to determine the frequencies of gestures and nonverbal communication as broken into the three mutually exclusive categories listed above. The coders specifically calculated the frequency of the child's initiating as well as responding behaviors that occurred across joint attention (JA) and behavioral requests (BR). Composite scores for joint attention were created by calculating the initiating and the responding joint attention behaviors (i.e. IJA + RJA). A similar composite score was calculated for BR (IBR + RBR). Finally, the total joint attention scores were calculated by combining the composite JA and BR scores (see Table 2). A criterion coder coded 25% of all the videos. The interrater reliability was considered to be sufficient with Cohen's Kappa coefficients of $\kappa = 0.78$ for Joint Attention behaviors, $\kappa = 0.75$ for Behavioral Requests, and $\kappa = 0.76$, for

Social Interaction behaviors. A total of 29 infants were not included for the assessment of joint attention scores at visit one due to their ages being outside of the validated assessment age ranges (e.g. ESCS for ages 8 months and older).

The Mullen Scales of Early Learning (MSEL; (Mullen, 1995). The MSEL is a standardized examiner administered developmental measure of language, cognitive, and motor functioning. The MSEL provides age-equivalent and standard scores from birth to 68 months of age. Five subscales were administered and included gross motor, fine motor, visual reception, expressive language, and receptive language. An overall standardized score of intellectual functioning known as the Early Learning Composite was also obtained. Computer calculated age-equivalent standardized scores were used for analysis from the five subscales and summarized in Table 2.

Vineland Adaptive Behavior Scales-II (Sparrow, Cicchetti, & Balla, 2005). The Vineland-II is a standardized measure for assessing adaptive behavior of individuals from birth to 90 years of age. This measure was administered to the parents by the examiner and assessed four subscales of development including Socialization (interpersonal relationships, play and leisure time, and coping skills), Communication (receptive, expressive, and written subdomains), Motor (fine and gross motor), and Daily Living skills (personal, domestic, and community subdomains). Standard scores were utilized for the subdomains in order to assess developmental adaptive skills (see Table 2).

MacArthur Communicative Development Inventory (CDI; Fenson et al., 1993). The CDI Words & Gestures form is a parent questionnaire that assesses aspects of language development, including gestures, words understood, and words produced by infants and toddlers. The CDI Words and Gestures form (eight to 16 months) assesses the child's responding to name, includes

a 396-item vocabulary checklist divided into 19 semantic categories, and rates the child's production of gestures as broken into early (games and routines) and later gestures (actions with objects, imitating adult actions, etc.). The CDI Words and Sentences form (16 to 30 months) was also utilized for the older toddlers in the study. The Words and Sentences form consists of a checklist of 680 words typically produced by English-speaking children. Additionally, the Words and Phrases section assesses grammar acquisition, whereby parents indicate their child's ability to combine words, provide examples of the three longest sentences, and complete questions related to sentence structures and morphemes the child produces. For the current sample, the majority of the participants were administered the CDI Words and Gestures form and 15 participants were administered only the Words and Sentences version (see Table 2).

Analytic plan

Eye-tracking Coding and Data Reduction. Raw eye-tracking data outputted from the Tobii Studio software was subsequently analyzed for fixation points using areas of interest (AOIs) in Noldus Observer XT Behavior Software. Independent coders scored frame-by-frame gaze behaviors into one of the seven AOI categories from raw superimposed gaze fixation data files. A total of 182 video clips (3873 frames per participant) were coded for the current study. A fixation was defined as a data point if it remained within a 30-pixel radius for a minimum of 100 milliseconds. The total on-screen area was divided into seven AOIs including: (1) the eye region of the actors; (2) the mouth and chin region; (3) the object region (candle, champagne bottle, etc.); (4) a face region (nose, cheeks, forehead, any area outside of the eyes and mouth); (5) hair; (6) body regions of the actors; and (7) an 'other' region that consisted of any gaze outside of the AOIs. Fixations were also coded for no gaze when the participants looked away from the stimulus displayed on the screen. Coders were trained to 95% agreement before independently

coding. Four coders scored the different gaze data and the interobserver reliability as calculated by the Intraclass Correlation Coefficient (ICC) for the AOI variables eyes, mouth, face, body, other, and objects was 90.6%, 91.4%, 90.2%, 93%, 94.3%, and 91.8%, respectively.

In order to examine differential gaze patterns during dynamic social scenes, the participants' fixation durations (i.e. total viewing time) were calculated. As infants differ in overall fixation duration (FD), proportion of total looking time (PTLT) was calculated for each individual AOI. Dependent variables were based on the amount of gaze on each AOI (eyes, mouth, face, body, hair, object, and other) divided by the total amount of on-screen looking time. Gaze towards the scene was calculated by the total amount of on-screen looking time divided by the scene duration. For each child, separate analyses were conducted for the AOI regions of eyes, mouth, and overall scene (i.e. these AOI regions served as dependent variables for longitudinal analyses).

Data from the eye-tracking and developmental questionnaires across the four time points (visit 1 to visit 4) were analyzed using multilevel models (MLM) for longitudinal designs in R 3.2.2 (citation package = nlme) to examine the eye gaze patterns of TD infants and toddlers. These models estimate individual growth trajectories and between-group differences in average levels of the outcome variables as well as trajectories of those variables over time (Singer & Willet, 2003). MLM postulate statistical models at two levels. A level one model depicts each infant's change trajectory (within-person age differences) with growth curve parameters such as the intercept and the slope. Simultaneously, a level two model describes the individual differences in the growth curve as a function of the predictors (between-person differences). As participant data was nested within time, using a MLM approach was beneficial for exploring not only where infants and toddlers began on their gaze and social attention, but also how their

growth trajectories changed as development progressed. Thus, time (i.e. visit) served as the level-1 predictor and contributors of gaze behaviors were examined as level-2 variables.

Results

The objective of this study was to evaluate the patterns of longitudinal change in the gaze behaviors of TD infants and toddlers. Specifically, we were interested in eye gaze behaviors, joint attention, and language skills that would explain the variability among individual growth trajectories.

Descriptive Analyses & Correlational Analyses

Table 2 provides the means and standard deviations for the developmental measures in the study across the four time points. After visually plotting histograms and checking for normality, some primary variables had high kurtosis values, which resulted in conducting Box-Cox power transformations (Box & Cox, 1964). All primary variables were person-centered for interpretability purposes. For instance, for the longitudinal analysis of the age variable, person-mean centering was applied due to an infant's age within his or her age group being more meaningful than the overall group mean of age. By doing so, we are also able to calculate more accurate estimates for within-group slopes (Bliese, 2006). Table 3 provides correlational analyses between all predictor and outcome variables. Pearson correlation results indicated strong positive relationships between visit and PTLT toward characters' mouth ($r = .25$, $p < 0.01$). Additionally, age was significantly correlated with gaze toward mouth ($r = .27$, $p < 0.01$), objects ($r = .17$, $p < 0.05$), as well as developmental assessments of joint attention ($r = .44$, $p < 0.01$), MSEL Receptive language ($r = .28$, $p < 0.01$), Vineland-II Communication ($r = .35$, $p < 0.01$), Socialization ($r = .35$, $p < 0.01$), and Adaptive ($r = .25$, $p < 0.01$) subscales. For an assessment of the infants' longitudinal gaze trajectories, a parallel plot of the gaze behavior data

as a function of visit is presented in Figure 2. Overall, infants' and toddlers' gaze behaviors and the rate of this change varied considerably across visits.

Multilevel Modeling Analyses

This analysis aimed to evaluate the eye gaze patterns of TD children from age three to 24 months. Additionally, the unique contributions of joint attention and language development skills were also modeled for predicting infants' rate of gaze behavior changes. To test the developmental predictions, a series of multilevel models were fit for the longitudinal data: First, three unconditional models were fit to examine the variability of eye gaze behaviors between and within participants as well as the mean and variability of the individual growth parameters (i.e. the intercepts and slopes). Second, a series of multilevel models with single level-two predictors were tested. These predictors included total joint attention scores, assessed from the ESCS, Communication and Socialization scores, measured from the Vineland-II, and Receptive and Expressive language scores, as assessed from the MSEL. Third, the random effect structure of the best multipredictor model: random intercept or random intercept and slope, was tested. Finally, the final model used the most parsimonious random effect structure (random intercept and slope) to test the developmental hypotheses.

Unconditional model for Overall Scene. The first step of the model development included fitting an unconditional means model (random intercept) and an unconditional growth model (random intercept and slope). The unconditional means model assumes that although infants vary in their gaze behaviors, each individual's developmental trajectory is flat and describes the variation in gaze behaviors. The unconditional growth model assumes that infants differ not only with regard to their initial gaze behaviors, but also with regard to their subsequent growth of gaze patterns. The results from the intraclass correlation coefficient (ICC) indicated that there

was 29% variance in the outcome variable of PTLT toward overall scene that was explained due to differences between infants and toddlers. The fixed effects of the unconditional growth model provided estimates for the intercept and the slope of the population average change trajectory. The results indicated that the estimated average infant displayed 69% of overall on-screen looking time at visit one (level-1 predictor). The visit variable did not significantly predict the infants' and toddlers' changes in overall PTLT toward scene ($p > .38$). Thus, the next step was to model for no random effect of visit, which meant that an infant's visit was measured without any error (i.e. fixed effect). The results indicated that the model didn't significantly improve as determined by the significant likelihood statistic and thus the random effect of visit was utilized for further model development. In order to see if an infant's age was a significant factor that explained the gaze changes over time (level-1 predictor), instead of visit, the unconditional means and growth models were re-conducted. The results indicated that age also did not contribute to changes in the average infant's total on-screen looking time ($p > 0.44$).

Predictor models and model development for Overall Scene. The second step of the model building included fitting a series of predictor models. Variables were entered simultaneously as predictors of infant's initial gaze behaviors and their subsequent rate of gaze behavior growth. Results indicated that the average infant's overall PTLT was not significantly predicted by total joint attention (TJA), MSEL Composite, the MSEL Receptive and Expressive subscales language subscales, and the Vineland-II Socialization and Communication subscales scores. That is, these predictors did not significantly contribute to the variations in infants' and toddlers' gaze behaviors over time. The interaction terms for these variables were also found to be non-significant in explaining the children's gaze trajectories over time.

In order to examine research question two and the specific parts of the face that infants and toddlers focused on, two separate analyses were conducted with PTLT toward eyes and PTLT toward mouth as the dependent variables.

Unconditional model for Gaze Toward Eyes. Results from the unconditional means and growth model indicated that the intraclass correlation coefficient (ICC) was 17%. This meant that 17% of the variance in the outcome variable of PTLT toward eyes was explained due to differences between infants and toddlers rather than within-person differences. Figure 3 provides an assessment of the infants' longitudinal gaze trajectories as a parallel plot with gaze behavior data toward eyes plotted as a function of visit. The fixed effects of the unconditional growth model provided estimates for the intercept and the slope of the population average change trajectory. The results demonstrated that the estimated average infant displayed 5% of their gaze toward eyes at visit 1. Visit (a variable of time) did not significantly predict changes in infants' gaze behavior toward eyes (b = .00; $t(104) = 1.28$, $p > .20$). Building upon the unconditional means model, a model with no random effect of visit was tested. The model with no random effect of time (visit) was more slightly favored in comparison to allowing the time variable to have a random component (i.e. measured with error and comes from a population distribution). Improvements in the model fit were evaluated by comparing fit statistics (-2 log likelihood or -2LL statistic) across nested models. However, based on previous findings and theory of development (see Jones & Klin, 2013; Elsabbagh et al., 2014), TD infants' growth trajectories in gaze behaviors are expected to vary over time; thus, visit (as a measure of time) was entered as a random effect in subsequent models.

Predictor models and model development for Gaze Toward Eyes. The second step of the model development included fitting a series of predictor models. Variables were entered as

predictors of infant's initial gaze behaviors toward eyes and their subsequent rate of gaze behavior growth. The first predictor entered alongside visit for an infant's gaze behavior toward eyes was age. Results demonstrated no significant effects for age (b = -.00; $t(103)$ = -.82, p > .42) or visit (b = .01; $t(103)$ = 1.38, p > .17) across time. The next step in the model building process included the main effects of visit, age, and the interaction term for visit and age. Results showed only a main effect of visit on the gaze behaviors of infants and toddlers towards eyes, (b = .01; $t(102)$ = 2.09, p < .04). This meant that with every new visit over time, controlling for age, infants and toddlers increased their gaze behaviors toward the characters' eyes by 4%. There was no significance found for age or the interaction term between age and visit.

For the final step of the model building, non-significant predictors were dropped and control variables of other AOI regions were added. Specifically, these variables included infants' and toddlers' gaze towards mouth, body, face, objects, and an other region along with age and visit. Results indicated that mouth (b = -.55; $t(97)$ = -7.43, p < .01), body (b = -.69; $t(97)$ = -10.56, p < .01), face (b = -.49; $t(97)$ = -10.38, p < .01), objects (b = -.31; $t(97)$ = -3.71, p < .01), and other (b = -.50; $t(102)$ = =12.58, p < .01) all significantly predicted children's changes in PTLT toward eyes. More specifically, the average infant's PTLT toward eyes at visit one when the infant is approximately 11 months old, with average PTLT toward predictors of mouth, body, face, objects, and other was 19%. Additionally, the interaction term for visit and age was not significant, ($F(1, 96)$ = 5.37, p > .05). The final model is provided in Table 4. The overall variance in infants' and toddlers' gaze trajectories explained by the final model was 68%. Visual inspection of the residual plots from the final model did not reveal deviations from homoscedasticity or normality.

Developmental assessments & gaze behaviors. In order to examine research question three about how the eye gaze patterns relate to developmental measures of joint attention, language development, and adaptive behaviors, MLM models were conducted. The steps of model building included specifying additional predictors of children's gaze behaviors with visit and age such as total joint attention (TJA), MSEL Composite and the MSEL Receptive and Expressive subscales, and the Vineland-II Socialization and Communication subscales. Due to model non-convergence, the MSEL Composite and the MSEL Receptive language variables were dropped due to their previous non-significant results (i.e. non-significance found when entered individually into the model). Thus, the model with visit as the level-1 predictor and age, total joint attention (TJA), MSEL Expressive language subscale, and the Vineland-II Socialization and Communication scores were entered as level-2 predictors for children's gaze PTLT toward eyes. The results indicated a significant main effect for visit ($b = .01$; $t(59) = 2.50$, $p < .05$), which meant that over time with each new visit, controlling for level-2 predictors such as the average age, infants and toddlers increased their gaze behaviors towards the characters' eyes by 2%. All other predictors of joint attention, language development, and adaptive skills did not significantly contribute to explaining children's growth pattern changes in PTLT toward eyes.

Unconditional model for Gaze Toward Mouth. The next set of MLM analyses included examining children's gaze trajectories and the dependent variable of PTLT toward mouth. The first step of the model development included fitting an unconditional means model (random intercept) and an unconditional growth model (random intercept and slope). The ICC indicated that 11% of the variance in children's gaze trajectories over time toward the actors' mouth was due to between-person differences. Figure 3 provides a parallel plot as an assessment of the

infants' longitudinal gaze trajectories toward mouth as a function of visit. The next step included running the unconditional growth model with visit as a random effect. Results indicated that visit was significant in explaining the change over time in infants' gaze behaviors towards the mouth (b = .01; $t(104)$ = -3.30, $p < .01$). More specifically, 3% was the average proportion of gaze allocated toward the actors' mouth by the average infant at visit one. For every new visit, the amount of gaze allocated towards the mouth went up by 1%. The fit for model one where visit was allowed to vary over time (i.e. random effect) was compared against the fit for a model without random effects. The loglikelihood ratio indicated the fit was better when visit was fixed and not allowed to vary. However, in order to support the developmental theory and previous findings on gaze behaviors, visit was allowed to vary for all subsequent models.

Predictor models and model development for Gaze Toward Mouth. The second step of the model development included fitting a series of predictor models. Variables were entered as predictors of infant's initial gaze behaviors and their subsequent rate of gaze behavior growth toward the mouth AOI region. Age was the first variable entered into the model and the results demonstrated that neither age (b = .00; $t(103)$ = 1.39, p = .17) nor visit (b = .00; $t(103)$ = .64, p = .52) significantly explained the variance in infants' and toddlers' PTLT toward mouth. The next approach for model building included adding in the age and visit interaction term. There was a non-significant interaction term found, $F(1, 102) = 4.83$ $p > .05$) for visit and age.

The final step in the model development included examining which variables specifically were independent predictors of the children's gaze behaviors toward the mouth AOI region. The AOI variables of eyes, body, face, objects, and other were incorporated into the model with age and visit. Results indicated that eyes, body, face, object, and other significantly predicted children's changes in gaze behavior patterns toward the actors' mouth. Results from these fitted

models are provided in Table 5. More specifically, the average infant's PTLT toward mouth at the first visit when the infant is approximately 11 months old, with average PTLT toward predictors of eyes, body, face, objects, and other was 11%. The final model was assessed for the variance explained and it indicated that 54% of the variance could be explained in children's gaze patterns toward the mouth over time when AOI predictors, age, and visit were accounted for. Visual inspection of the residual plots from the final model did not reveal deviations from homoscedasticity or normality.

Developmental assessments & gaze behaviors. Relevant level-2 predictors were incorporated into the model such as total joint attention (TJA), Vineland-II Socialization and Communication subscale scores, and the MSEL Receptive and Expressive language scores, along with the interaction term for visit and age. Results indicated that these predictors were not significantly accounting for the infant's and toddler's PTLT toward the actors' mouth.

Discussion

The measurement of young children's gaze behaviors unveils developmental processes that facilitate recognizing and influencing the social behaviors of others (Beier & Spelke, 2012; Leppänen, 2016). Studies portraying dynamic stimuli that mimic everyday social interactions within an eye-tracking paradigm allow for simultaneous processing of gaze behaviors as well as the underlying visual attention processes. The current study addressed the importance of measuring longitudinal gaze trajectories in TD infants to serve as a comparison proxy for high-risk infant groups. More recent studies have advocated for the development of typical social scene scanning as an important precursor for early identification of at-risk social behaviors (Boyd, Odom, Humphreys, & Sam, 2010; Jones & Klin, 2013); thus creating the need to provide longitudinal evidence of typical gaze trajectories across dynamic scenes.

The objective of the current study was to evaluate the gaze patterns of longitudinal change in 30 TD infants and toddlers during dynamic social scenes from three to 24 months of age. Furthermore, the longitudinal gaze trajectories were assessed with their relations to developmental measures of joint attention, language development, and adaptive behaviors. Research question one explored the overall eye gaze behaviors of infants and toddlers during audio and video stimuli, as measured by the proportion of total looking time (PTLT). We hypothesized that infants and toddlers would display longer fixation durations for human characters over objects. Results from the multilevel modeling indicated that changes in visit and age were not significant in accounting for the differences in overall PTLT toward scene. Furthermore, key predictors of developmental measures such as joint attention and language development also did not contribute to gaze trajectory changes for overall PTLT for scene for the current sample. Although the results from this study did not support the original hypothesis, the study highlights how the overall differences in infants' proportional fixation durations for dynamic stimuli can be dependent on the contextual environment. Previous studies have reported that irrespective of age, infants exhibit clear differences in gaze behavior towards faces versus other objects, depending on the visual context in which it arises (Beier & Spelke, 2012; Elsabbagh et al., 2014). Although gaze behaviors across static stimuli have been widely studied among infants (Easterbrook et al., 1999; Gredebäck et al., 2010; Grossmann & Johnson, 2010; von Hofsten et al., 2005), much less is known about how infants allocate their visual attention within dynamic stimuli that demand both auditory attention and faces embedded within heterogeneous scenes. Thus, a contribution of this study is that few studies have utilized moving or talking faces as dynamic stimuli for understanding gaze patterns in infants as early as three

months of age, despite the fact that these dynamic interactions represent real world situations in which infant gaze behaviors develop.

The non-significant differences found in the PTLT toward overall scene over time in the current study may reflect the fact that infants' visual experiences are a complex interplay of simultaneous development and social processing. For instance, in general, young infants have predominantly non-relevant gaze following behaviors at two and six months (Gredebäck et al., 2010, 2009), which gradually shifts towards more consistent use of gaze understanding and following between four and eight months of age. It is possible that although younger infants are oriented from birth toward the gaze of interesting social partners, they may require more specific ostensive cues such as speech and direct gaze in order to fixate on socially relevant partners (Guellai & Streri, 2011; Senju & Csibra, 2008). In sum, as the social functions of human gaze are considered to be quite diverse, ranging from following one's gaze to inferring mental states (Guellai & Streri, 2011; Jones & Klin, 2013), it is critical that infants master others' gaze behaviors and allocate attention to allow them to develop and refine their socio-cognitive skills.

Hypothesis two and three focused on examining the different gaze behaviors toward face, particularly the eyes and mouth and its relations to joint attention and language development. Results from the MLM analyses indicated that overall visit or time influenced infants' gaze behaviors toward eyes and mouth above and beyond gaze allocated to other AOI regions. The results indicated that overall there were differences in how infants viewed the AOI regions of eyes and mouth as well as gaze differences across the social actors over time. Previous research has shown that eye gaze seems to modulate face recognition fairly soon after birth (Carver et al., 2003; Farroni et al., 2002; Guellai & Streri, 2011), supporting an innate, dependent system devoted to gaze processing that orients newborns' sensitivity to faces and the social signals

conveyed by the eyes (Hoehl et al., 2009), and that continues to develop across the first year of life as infants (Frank et al., 2009; Hunnius & Geuze, 2004). This finding was supported in the current study in that infants' gaze behaviors toward the eyes AOI changed over time. This is also expected due to neurodevelopmental attentional biases changing as the visual cortex system develops and specializes over the first year of life (Brooks & Meltzoff, 2005; Elsabbagh et al., 2014; Gredebäck, Theuring, Hauf, & Kenward, 2008). This also explains why gaze behaviors in the current study were related to the visit as opposed to the age of the infant. Similarly, these infants are becoming increasingly proficient at processing dynamic cues presented from complex scenes and are more sensitive to intersensory redundancy, such as matching between speech sounds and moving mouths (Senju & Csibra, 2008; Stoesz & Jakobson, 2014); thus, having more refined gaze behavior changes toward the eyes and mouth regions.

Despite multiple studies on behavioral measures of gaze processing, it is still unclear exactly why infants allocate differences in gaze towards specific areas of the face and its subsequent impact on social attention. For instance, it has been suggested that although infants' preferential tracking of the eyes may attract their attention in complex scenes, an interest towards the mouth between the ages of four and eight months is also normative, as it could be reflective of the acquisition of pre-verbal skills (Elsabbagh et al., 2014; Stagg, Linnell, & Heaton, 2014). The current study's significant results related to the changes in PTLT toward eyes and mouth, influenced by time, could be indicative of the acquisition of pre-verbal skills as children develop and age coincides with the emergence of language production (Tenenbaum et al., 2013; Wagner et al., 2013).

The significant differences found in the infants' and toddlers' gaze trajectories toward the mouth reflect the highly salient nature of the mouth, especially a talking mouth. This is in

corroboration with previous studies indicating fixations to the mouth can be related to language acquisition and processing (Hillairet de Boisferon et al., 2016; Lewkowicz & Hansen-Tift, 2012; Tenenbaum et al., 2013). Finding significance in the infants' PTLT changes for the AOI regions of eyes and mouth over time may imply that gaze behaviors could be dependent on the contextual environment and/or the saliency of the visual scenes. The allocation of gaze to different stimuli across the face is also influenced by social cognitive motives that use others' gaze direction and the social context within which social interactions take place in order to detect communicative acts (Augusti, Melinder, & Gredebäck, 2010). The extant literature on infants' selective attention to focus on the talker's mouth is consistently found (Frank et al., 2009; Lewkowicz & Hansen-Tift, 2012; Parise et al., 2010). More specifically, gaze behaviors of infants and toddlers may become more established and use more refined visual capabilities through experience-dependent processes that allow for more focus toward one social region over another (i.e. if the actor is holding salient objects or is carrying communicative facial expression cues) (Elsabbagh et al., 2013; Gredebäck et al., 2008; Young et al., 2009).

Research question three examined how gaze behaviors were related to the developmental measures of joint attention, language skills, and adaptive behaviors. We hypothesized that there would be positive associations between gaze behaviors, joint attention, and early language skills over measured key developmental periods. The results from the current longitudinal analyses did not show joint attention, language, or other adaptive behaviors influencing infants' and toddlers' changes in gaze trajectory toward the eyes or mouth. Previous research has shown the importance of joint attention, gaze behaviors, and early language acquisition, as these behaviors serve as deictic social cues and nonlinguistic scaffolding during adult-child interactions (Jones & Carr, 2004; Krstovska-Guerrero & Jones, 2013; Mundy et al., 2007; Navab et al., 2012; Swanson

& Siller, 2013). This study is among the few to begin examining simultaneous associations between gaze trajectories to the eyes and mouth, joint attention, and language development across the first two critical years of development. More empirical studies need to be conducted in order to adequately explain the processes that underlie the infants' ability to initiate and respond to joint attention within the first year of life. For instance, empirical studies on joint attention suggest that a preference to look at the eyes around the age of six months reflects the mere observation of the attention of others (Mundy et al., 2007; Mundy & Gomes, 1998). Later this skill becomes integrated with self-attention, leading to initiating JA skills at the age of 12 months, and thus supporting the idea that triadic abilities build on earlier dyadic and responding JA skills (Grossmann & Johnson, 2010; Schietecatte, Roeyers, & Warreyn, 2012).

Overall, the results of the present study emphasized the importance of understanding gaze behaviors and their changes in infancy in order to understand the underpinnings of joint attention and language development (Reid, Striano, Kaufman, & Johnson, 2004; Schietecatte et al., 2012; Swanson & Siller, 2013). Gaze behaviors modulate and shift across the first year of life, from preferences for direct gaze as neonates to more flexible JA skills by the end of the first year (e.g., Bedford et al., 2014; Navab et al., 2012); thus increasing the likelihood of observing concurrent relationships between JA, language, and gaze behaviors during this key developmental time period in comparison to other developmental periods. Although the current study did not find statistically significant relations in the gaze patterns of longitudinal change in infants and toddlers and their joint attention, language, and adaptive skills, the development of advanced social skills as fostered by gaze behaviors during infancy continues to be in need of further understanding.

Limitations & Conclusions

The present study had a few limitations that affected the generalizability of the results. First, the sample size was still relatively small and might have reduced the power to detect statistically significant effects for observing longitudinal change. However, the current sample size is comparable with other studies that employ eye-tracking technology (Gredebäck et al., 2009; Hayhoe, 2004) due to the large amount of gaze fixation data that is produced. Furthermore, obtaining a more diverse sample that is representative of different demographics might be more generalizable. Second, one of the biggest challenges in the current study was the attrition rate that is often common in infant studies with longitudinal designs. However, including different participants to assess changes in social attention, gaze behavior, and language development has provided us with important information of the mechanisms taking place across developmental trajectories. Third, due to the challenging nature of obtaining reliable measures in infant research, the dynamic stimulus utilized may be a confounding factor for the study. This may have led to differences in gaze behaviors due to the novelty of the complex stimuli itself, rather than the underlying nature of social attention and fixation patterns. However, all participants were exposed to the same dynamic stimuli in the same controlled lab setting, and this type of realistic stimulus involving a human provided for a more potent ecological design.

Overall, there are several significant contributions of this work. First, this study is among the first few studies to rely on dynamic stimuli with high precision eye-tracking technology to represent longitudinal eye gaze patterns of TD infants and toddlers within the first two years of life (see Frank et al., 2009; Gredebäck et al., 2010, 2008; Senju & Csibra, 2008). Second, by virtue of following infants over key developmental periods, this study examined targeted relationships between social attention, joint attention, and language development that have often been considered independently, but not carefully delineated simultaneously (Hamilton, 2015;

Meltzoff & Kuhl, 2016). There is an increasing interest in understanding the developmental course of eye gaze behaviors in human infants and the deviations from these typical trajectories as potential endophenotypic markers of certain neurodevelopmental disorders (Ahtola et al., 2014; Elsabbagh & Johnson, 2010). The current study provided evidence for the importance of tracking longitudinal gaze patterns in very young infants utilizing innovate methodologies and analytic techniques. The findings from this study suggest that research using dynamic eye-tracking methods shed light on the complexity of the visual world as mediated by the infant's ability to systematically attend to and alter gaze to the different social signals of the stimulus.

Table 1.

Descriptive information about typically developing sample at study entry and across longitudinal visits

	Time 1	Time 2	Time 3	Time 4
Age Group (Range)	*N* = 73	*N* = 45	*N* = 36	*N* = 30
3-month-olds (± 1 month)	16	-	-	-
6-month-olds (± 1 month)	14	13	-	-
9-month-olds (± 1 month)	14	16	09	-
12-month-olds (± 1 month)	13	12	16	09
14- to 24-month-olds (9 months)	16	04	11	21
Males: Females	41:32	26:19	21:15	17:13
Child's Race				
Asian	1 (1.4%)	-	-	-
Black or African American	1 (1.4%)	1 (2.2%)	1 (2.8%)	1 (3.3%)
White	56 (76.7%)	34 (75.6%)	27 (75%)	22 (73.3%)
Mixed/ Other	10 (13.7%)	6 (13.3%)	5 (13.9%)	5 (16.7%)
Maternal Education: N (%)				
High School/GED	5 (6.8%)	4 (8.9%)	4 (11.1%)	3 (10%)
Some College	8 (11%)	4 (8.9%)	3 (8.3%)	3 (19%)
Associate's Degree	4 (5.5%)	2 (4.4%)	2 (5.6%)	2 (6.7%)
Bachelor's Degree	21 (28.8%)	11 (24.4%)	8 (22.2%)	7 (23.3%)
Graduate Degree	35 (47.9%)	24 (53.3%)	19 (52.8%)	15 (50%)
Marital Status N (%)				
Single, never married	14 (19.2%)	8 (17.8%)	6 (16.7%)	6 (20%)
Married	55 (75.3%)	35 (77.8%)	29 (80.6%)	23 (76.7%)
Divorced	3 (4.1%)	1 (2.2%)	-	-
Widowed	1 (1.4%)	1 (2.2%)	1 (3.3%)	1 (3.3%)

Table 2.

Means and standard deviations of developmental assessments at each wave of data collection

Assessment	*Visit 1* *N = 73* *M (SD)*	*Visit 2* *N = 45* *M (SD)*	*Visit 3* *N = 36* *M (SD)*	*Visit 4* *N = 30* *M (SD)*
Age	9.44 (5.185)	10.02 (3.92)	12.64 (2.63)	15.50 (2.80)
Mullen Scales of Early Learning[1]				
Receptive	50.01 (10.98)	50.29 (9.86)	50.03 (11.29)	47.00 (9.07)
Expressive	52.03 (10.03)	53.29 (8.65)	55.83 (10.17)	53.47 (8.16)
Gross Motor	54.12 (10.89)	56.76 (8.87)	57.83 (9.72)	53.90 (9.06)
Fine Motor	54.09 (10.11)	52.67 (8.37)	55.50 (10.87)	50.67 (11.16)
Visual Reception	52.67 (11.43)	50.07 (11.77)	53.17 (11.61)	43.37 (9.67)
Early Learning Composite	104.49 (15.74)	103.18 (14.82)	107.03 (17.47)	97.53 (13.22)
Early Social Communication Scales[2]	*N = 46*	*N = 32*		
Total Joint Attention Scores	38.02 (16.32)	38.70 (12.02)	47.63 (16.11)	49.53 (16.80)
Joint Attention	25.74 (11.07)	24.88 (9.18)	28.60 (10.24)	26.42 (11.29)
Behavioral Requests	12.28 (9.49)	13.83 (8.03)	18.97 (9.67)	23.12 (8.92)
MacArthur Child Development Inventory	*N = 39*[3]*; N = 4*[4]	*N = 30*[3]*; N = 2*[4]	*N = 35*[3]*; N = 1*[4]	*N = 21*[3]*; N = 9*[4]
Words Understood[3]	74.51 (71.07)	48.43 (44.25)	83.40 (66.17)	140.71 (78.99)
Words Understood Percentile[3]	39.36 (26.63)	38.01 (29.32)	37.15 (27.56)	49.07 (23.36)
Words Produced[3]	9.82 (17.00)	3.80 (5.40)	9.74 (14.00)	33.91 (42.64)
Words Produced Percentile[3]	47.17 (20.41)	46.32 (22.81)	39.04 (27.56)	53.85 (23.83)
% Total Gestures[3]	45.05 (24.23)	50.25 (22.90)	50.02 (28.31)	61.37 (27.52)
Words Produced Percentile[4]	66.90 (30.97)	50.75 (56.78)	66.32 (-)	36.27 (15.14)
Mean Length in morphemes Percentile[4]	61.73 (31.92)	65.35 (28.78)	66.70 (-)	35.50 (29.81)
Vineland Adaptive Behavior Scales-II	*N = 70*			
Communication	105.83 (13.17)	104.47 (10.68)	105.33 (9.70)	101.40 (5.82)
Socialization	106.32 (15.07)	104.40 (10.15)	102.57 (7.05)	99.03 (6.48)
Motor skills	99.55 (15.70)	102.07 (11.55)	102.68 (11.03)	95.83 (9.57)
Daily living skills	107.16 (15.79)	106.00 (11.17)	109.90 (10.70)	107.90 (9.38)
Adaptive skills	105.31 (13.07)	104.70 (9.78)	106.24 (8.57)	100.97 (6.22)

Note. [1]Age equivalent scores. [2]Initiating and responding scores. Total Joint Attention = Composite score of JA + BR. [3]CDI Words & Gestures. [4]CDI Words & Sentences.

Table 3.

Correlations between all predictor and outcome variables at visit one

Variable	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
1. Visit	-	.46**	-.80	-.10	.18*	.25**	.17*	.30*	.09	.06	.25*	-.05	.11	-.06
2. Age		-	.28**	.10	.35**	.35**	.25**	.44**	.08	.02	.27**	-.15	.12	.17*
3. MSL_RL[1]			-	.51**	.28**	.13	.27**	.04	-.09	.04	-.10	.02	-.04	-.02
4. MSL_EL[1]				-	.11	.04	.13	.12	-.03	.01	.05	.09	-.02	.11
5. COMM[2]					-	.31**	.71**	-.14	-.10	.10	-.15	.22*	-.10	.17*
6. SOC[2]						-	.68**	-.21*	-.01	-.03	-.16*	.19*	-.06	.08
7. ADAPB[2]							-	-.25**	-.13	-.04	-.14	.22*	-.14	.19*
8. TJA[3]								-	.01	-.03	.06	.05	-.10	.10
9. Scene									-	.36**	.17*	-.25**	.34**	-.10
10. Eyes										-	.05	-.34**	.22**	-.17*
11. Mouth											-	-.17	.09	.06
12. Body												-	-.45**	.13
13. Face													-	-.20*
14. Objects														-

Note. [1]Age equivalent MSEL Receptive & Expressive subscale scores. [2]Vineland-II standard scores. [3]Initiating and responding Early Social-Communication joint attention scores. Total Joint Attention = Composite score of JA + BR.
*p <0.05. **p <0.01

Table 4.

Parameter estimates of the fixed effects from the final multilevel model of random intercept and slope models with gaze towards eyes as the outcome variable

Variable			
Fixed effects	*Intercepts*	*SE*	*t-value*
Intercept	.19***	.02	9.70
Visit	.01	.01	1.25
Age	-.00	.00	.47
Visit * Age	-.00	.00	-1.55
Mouth	-.55***	.07	-7.43
Body	-.69***	.06	-10.56
Face	-.49***	.05	-10.38
Objects	-.31***	.08	-3.71
Other	-.49***	.03	-12.58

$*p < 0.05$. $**p < 0.01$. $***p < 0.001$

Table 5.

Parameter estimates of fixed effects from the final multilevel model of random intercept and slope models with mouth as the outcome variable

Variable			
Fixed effects	*Intercepts*	*SE*	*t-value*
Intercept	.11***	.01	13.95
Visit	-.00	.00	-.15
Age	.00	.00	1.78
Visit * Age	-.00	.00	-1.54
Eyes	-.27***	.02	-13.30
Body	-.28***	.02	-12.30
Face	-.28***	.02	-15.97
Objects	-.26***	.03	-9.60
Other	-.30***	.01	-20.76

$*p < 0.05$. $**p < 0.01$. $***p < 0.001$

Figure 1. Still frames from video excerpt of *The Muppets Movie*

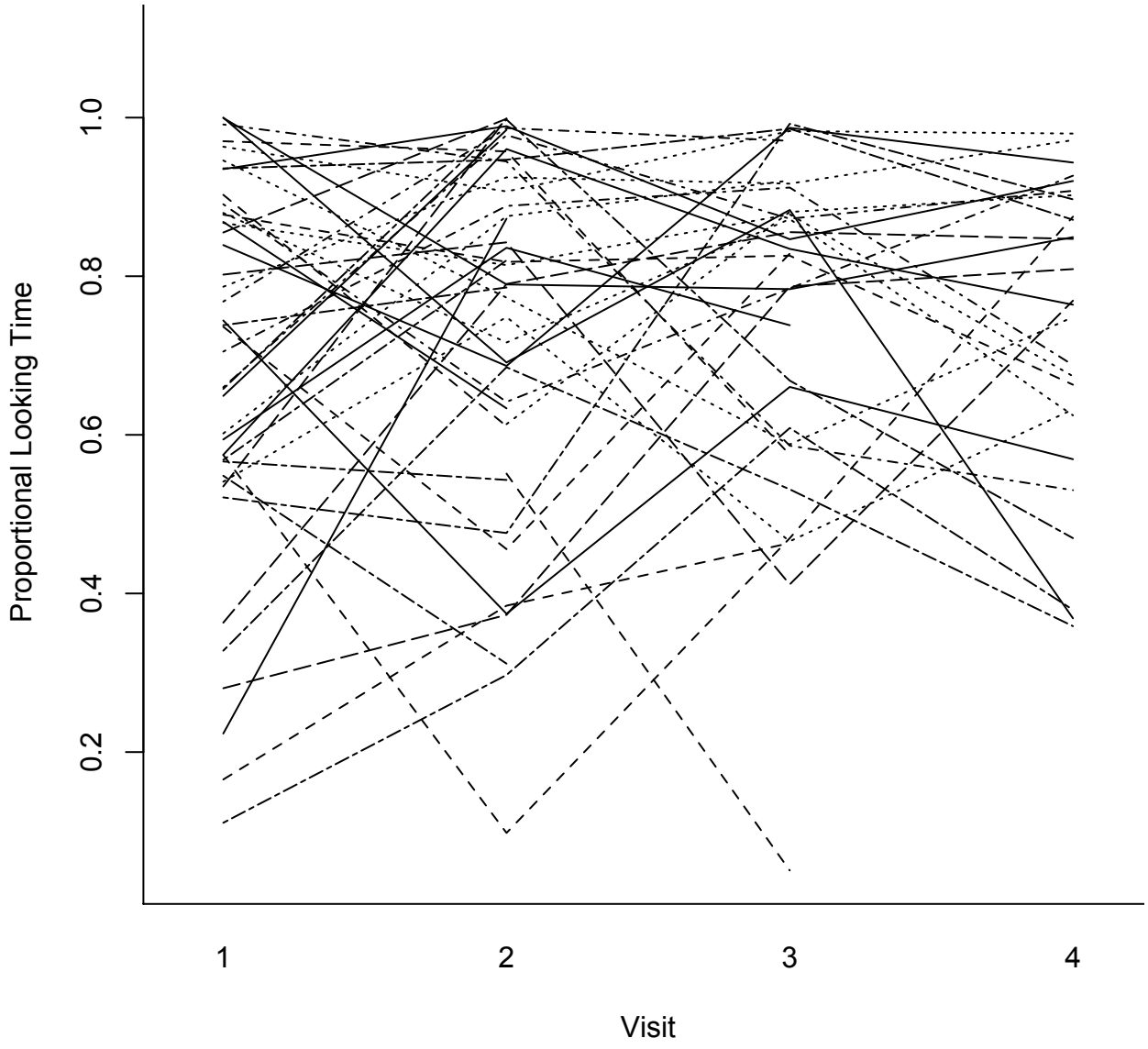

Figure 2. Parallel plot of proportional looking time as a function of infants' visits.

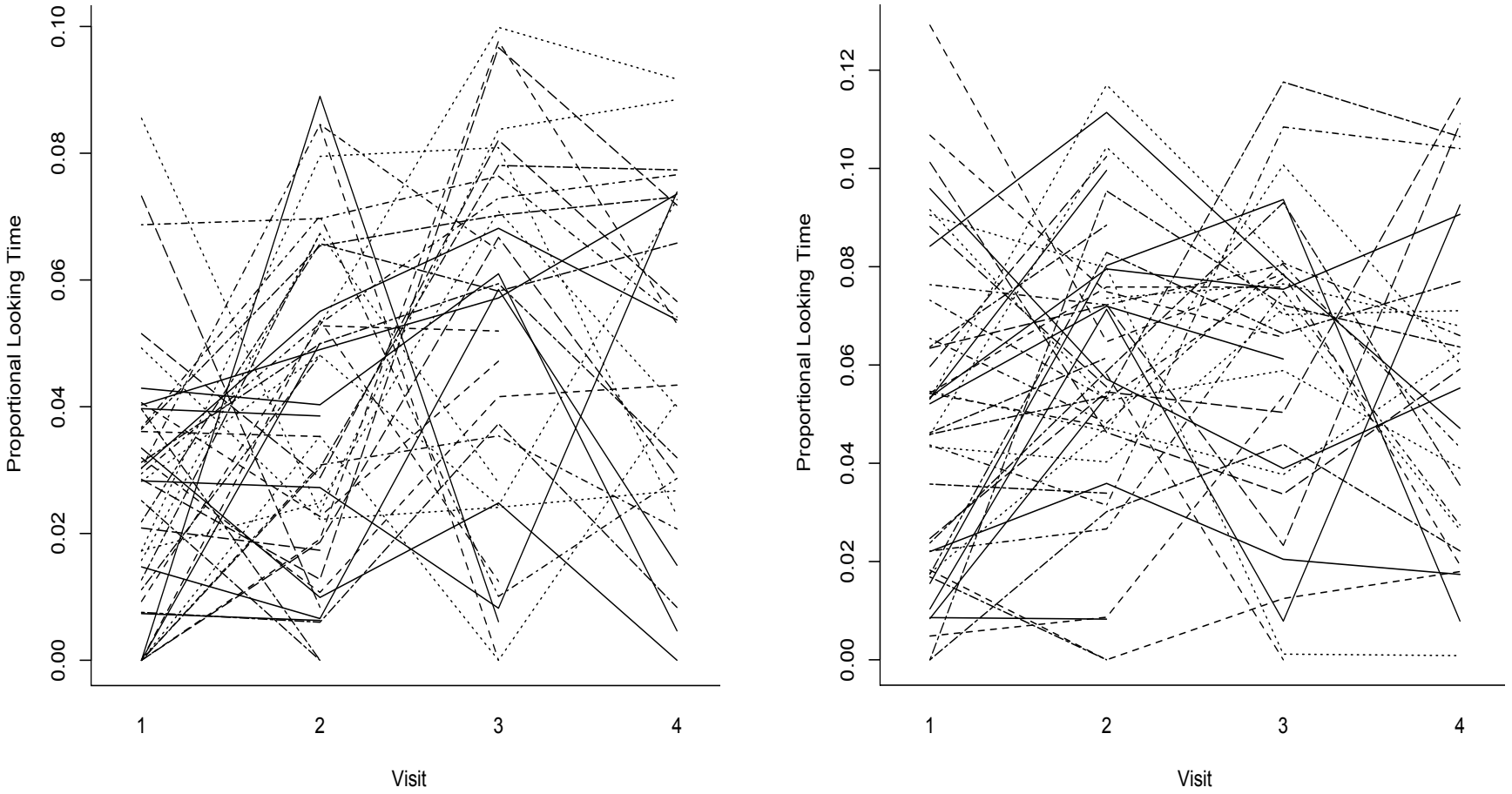

Figure 3. Parallel plots of proportional looking time towards mouth and eyes as a function of infants' visits.

CHAPTER III: VISUAL SOCIAL ATTENTION IN AT-RISK INFANTS AND TODDLERS: A LONGITUDINAL EXAMINATION OF GAZE PATTERNS

In the first year of development, a typical infant possesses basic orienting mechanisms that support preferential attention to social stimuli such as human faces (Chita-Tegmark, 2016b; Elsabbagh & Johnson, 2016; Leppänen, 2016). Human faces are perceived as one of the most relevant stimuli for typical infants leading to the development of crucial language and socio-communication skills (Brooks & Meltzoff, 2005; Mundy et al., 2007; Pelphrey et al., 2002). However, an increasing number of studies have described atypical attentional processing and recognition of faces across the lifespan in infants later diagnosed with autism spectrum disorders (ASD) (Ames & Fletcher-Watson, 2010; Chita-Tegmark, 2016a; Keehn, Vogel-Farley, Tager-Flusberg, & Nelson, 2015; Papagiannopoulou, Chitty, Hermens, Hickie, & Lagopoulos, 2014). Specifically, infants at-risk for ASD, due to having an older sibling diagnosed with ASD, display atypical attention to social stimuli such as reduced attention to faces and increased attention to bodies (Chita-Tegmark, 2016b; A Klin, Jones, Schultz, Volkmar, & Cohen, 2002). Additionally, these at-risk infants display inconsistent attention to different components of the social stimuli itself (Guillon et al., 2014; Pierce et al., 2016). Other abnormalities have also been described in facial processing and biological motion processing among infants at-risk for ASD (Katarzyna Chawarska, Macari, & Shic, 2013; A Klin, Lin, Gorrindo, Ramsay, & Jones, 2009; Nele et al., 2015).

Despite these known social atypicalities, characterizing an ASD-specific risk phenotype during infancy is challenging (Elsabbagh & Johnson, 2016; Rogers, 2009). However, the early assessment of infants' gaze behaviors allows for the investigation of any abnormalities within neurodevelopmental systems that may not be overtly recognized by parents or caregivers

(Elsabbagh & Johnson, 2010; Zwaigenbaum et al., 2005). Moreover, these prospective designs that pose differential hypotheses as related to behavioral risk markers with at-risk infants have been promising (Pierce, Glatt, Liptak, & McIntyre, 2009; Zwaigenbaum et al., 2009).

Infant Siblings of Children with ASD

Two seminal studies on the recurrence estimates among infant siblings of children with ASD (Messinger et al., 2015; Ozonoff et al., 2011) found a 19.5% recurrence rate for ASD across 15 different study sites. More specifically, the highest recurrence rates were seen among males (~ 27%) and in children with more than one older sibling diagnosed with ASD (~32%). For community-based samples on sibling and familial recurrence risk, the rate for ASD among full siblings was reported closer to 7% - 10% (Sandin et al., 2014; Szatmari et al., 2016). The investigation of detecting early "red flags" of ASD through ongoing monitoring of these at-risk infants is encouraging not only due to the high recurrence rates, but also for the need to inform families who use these estimates as benchmarks for their reproductive decisions. In addition, infant siblings and relatives genetically linked as high risk for ASD can manifest a wide variety of clinical and sub-clinical traits known as the broader autism phenotype (BAP). The BAP is characterized by issues surrounding social relatedness, communication deficits, and specific interests that vary in severity and co-occurrence (Elsabbagh et al., 2012; Elsabbagh & Johnson, 2010; S. Rogers, 2009). With multiple aspects of development affected by ASD among at-risk infant siblings, there continues to be a critical need for identifying the atypical characteristics that specify the risk for manifesting ASD and the concomitant social attention deficits (Boraston & Blakemore, 2007; Elsabbagh & Johnson, 2016; Zwaigenbaum et al., 2009).

Social Attention in Infants at-risk for or with ASD. Social attention studies have highlighted the importance of the context within which social stimuli is presented as well as how

the infants' attentional biases interact early on to regulate eye gaze behaviors (Falck-Ytter, Bölte, & Gredebäck, 2013; Guillon et al., 2014; Merin, Young, Ozonoff, & Rogers, 2007). Multiple studies on social attention and altered gaze patterns in at-risk infants have been able to show distinct impairments and/or delays in the following: (1) reduced eye-contact and gaze monitoring; (2) decreased flexibility in disengagement and shifting of attention; and (3) visual atypicalities such as prolonged visual tracking of objects (Ames & Fletcher-Watson, 2010; Elsabbagh & Johnson, 2010; Guillon et al., 2014; Landa, Holman, & Garrett-Mayer, 2007; Sally Ozonoff, Heung, Byrd, Hansen, & Hertz-Picciotto, 2008). More specifically, Chawarska and colleagues (2013) found that lower levels of overall looking time at social stimuli in six-month-old infants were associated with a later diagnosis of ASD. The 67 high-risk infants exhibited diminished gaze patterns in general to the social scene with less time spent monitoring the experimenter and her face. The study also did not find enhanced attention to the toys across the different conditions, demonstrating that atypical attentional responses at this age may still be poorly differentiating across visual scenes (Chawarska et al., 2013).

Shic and colleagues (2014) further examined the effects of context and looking at faces in 99 6-month-old high- and low-risk infants. Through the presentation of three conditions: (a) a static image, (b) a dynamic video of an actress smiling, and (c) a dynamic video of an actress speaking a nursery rhyme, the authors found that infants who later developed ASD looked less at the overall scene in comparison to low-risk infants. Furthermore, the authors stated that infants who later developed ASD showed reduced attention to not only static, but also to dynamic faces, with overall less looking at the socially informative inner features of the face (Shic, Macari, & Chawarska, 2014). Results from these studies demonstrate that at-risk infants display some heterogeneity in their attentional biases towards social and non-social stimuli. Some of these

attentional differences may be attributed to the variety of stimuli (i.e. static versus dynamic) and the differing experimental procedures used (Frank et al., 2014; Gredebäck et al., 2009). These findings are important because how well a stimulus approximates real-world social interactions impact the at-risk infants' abilities to accurately interpret eye contact, facial expressions, and gaze direction, which subsequently forms the groundwork for adaptive, social, causal, and cultural learning (Bal et al., 2010; Meltzoff, Brooks, Shon, & Rao, 2010; von Hofsten et al., 2005).

Facial Processing, Joint Attention, & Language. Longitudinal studies have shown that infants who later develop ASD show reductions in social responsiveness, atypical visual orienting, and reduced attention towards social stimuli by the end of their first year (Elsabbagh et al., 2013; Jones, Gliga, Bedford, Charman, & Johnson, 2014). For instance, Jones and Klin (2013) conducted a prospective, longitudinal eye-tracking study with 110 high- and low-risk infants to assess attention to eyes versus other areas of the face and body. The authors reported that very early in development (i.e. first month of life), both low-risk and high-risk infants displayed normative levels of attention to eyes. However, high-risk infants demonstrated a steady decline starting from four months and reached a level that was approximately half of that of low-risk infants by 23 months (Jones & Klin, 2013). Taken together, these prospective designs demonstrated atypical developmental disturbances during the first year of life that would not normally be detected clinically until a later age (Charman, 2014; Pierce et al., 2009). In a seminal eye-tracking study conducted by Merin and colleagues (2007), 31 six-month-old at-risk and 24 TD infants were assessed using a modified version of the Still Face paradigm. The authors found that a subgroup of at-risk infants demonstrated reduced gaze to their mother's eyes and increased gaze to her mouth areas. In a follow-up study, this increased attention to the mouth areas was

later associated with the six-month-olds' relationship to expressive language skills at 24-months (Young et al., 2009).

In any given interaction examining social attention, eye gaze can be subtle; thus assessing infants' moment-by-moment processing and gaze following abilities can have direct consequences for understanding individual differences in the infant's social engagement, language, and, in particular, joint attention skills (Navab et al., 2012; von Hofsten et al., 2005). Joint attention refers to the ability to engage in shared attention with others in order to establish a joint frame of reference for exchanging meaningful information (Jones & Carr, 2004; Mundy et al., 2007). Despite typically developing infants being able to swiftly respond to changes in others' gaze shifts by their first birthday (Gredebäck et al., 2010, 2008), infants at-risk for ASD display attentional atypicalities towards social stimuli (Ames & Fletcher-Watson, 2010; Frischen et al., 2007). This lack of social attention among children with ASD is important to understand as it impacts the higher-level cognitive skills such as joint attention, theory-of-mind, and language development (Adamson, Bakeman, Deckner, & Romski, 2008; Ames & Fletcher-Watson, 2010; Brooks & Meltzoff, 2005; Mundy et al., 2016). For instance, Chawarska and colleagues (2012) found that in an eye-tracking study with 13-to 25-month old toddlers with autism, developmental delay, and TD, conditions when there was no eye contact and speech (sandwich and moving toys condition), toddlers with autism showed similar attention towards the social scene as their TD counterparts. However, during the dyadic condition, where child-directed speech and eye contact were present, toddlers with autism displayed diminished attention to the overall scene with less monitoring of the speaker's face and her mouth. The study also found that atypical language profiles were associated with an overall decreased monitoring of the speaker's face and her mouth (Chawarska, Macari, & Shic, 2012). While some studies have demonstrated preliminary

evidence of atypical social and joint attention as prodromal or emerging autism symptoms, it is critical to continue investigating longitudinal trajectories of visual attention among at-risk infants.

In conjunction with atypical gaze behaviors towards social stimuli and faces, typical gaze following is considered a pivotal point for joint attention and socio-communicative development. More recently, Thorup and colleagues (2016) assessed the gaze following of 47 high-risk and 17 low-risk 10-month-old infants in an eye-tracking study. In the two conditions, the experimenter moved either (a) both the eyes and the head toward the objects (Eyes and Head condition) or (b) moved the eyes only (Eyes Only condition). These results indicated that the high-risk infants were less likely to follow the experimenter's gaze in the Eyes Only condition in comparison to the Eyes and Head condition. Furthermore, the low-risk infants did not differ between the two conditions, highlighting that without the verbal cues present, many high-risk infants for ASD display altered orienting patterns toward social stimuli (Thorup, Nyström, Gredebäck, Bölte, & Falck-Ytter, 2016). This study highlights the need for understanding infants at-risk for or with ASD's gaze behaviors and the context of directional gaze cueing, as it facilitates key developmental aspects of joint attention and language acquisition.

In sum, studies utilizing eye-tracking technology have highlighted behavioral differences during infancy related to social attention and communication among at-risk infants. Many eye-tracking studies have found reduced eye-contact and gaze monitoring, decreased flexibility in disengagement and shifting of attention, prolonged visual tracking of objects, and issues with social-communication such as social smiling, reactivity, and reduced expressions of positive emotions in infants later diagnosed with ASD (Elsabbagh et al., 2014; Jones & Klin, 2013; Zwaigenbaum et al., 2005, 2007).

Present Study

Research studies with infant siblings and dynamic eye-tracking stimuli are only recently breaking ground (Falck-Ytter et al., 2013); thus, there is a renewed sense of the importance in the study of longitudinal patterns of eye gaze and social attention in younger at-risk populations (Elsabbagh & Johnson, 2016). Additionally, it is important to examine and map the onset of abnormalities in visual attention, as these are considered to be early warning signs of risk behaviors in ASD (Falck-Ytter et al., 2013; Pierce et al., 2016; Zwaigenbaum et al., 2005). Adopting a longitudinal perspective can aid in identifying any behaviors that may indicate developmental deviations during infancy, a period known to be a critical window of development (Gredebäck, Fikke, & Melinder, 2010; Rogers & Talbott, 2016). As infants do not provide vocal affirmations of their gaze, it is through the use of dynamic stimuli in eye-tracking models that researchers can truly begin to explicate infants' gaze behavior patterns and information processing of social stimuli (Ahtola et al., 2014; Guillon et al., 2014).

The present study is guided by the following central research questions:

(1) What are the longitudinal eye gaze patterns of at-risk infants and toddlers during dynamic social scenes from three to 30 months?

(2) What are the regions of the face at-risk infants and toddlers focus on and how do these change over time?

(3) How do these eye gaze patterns relate to developmental measures of joint attention, language development, and adaptive behaviors?

I expect to find that, with age, at-risk infants and toddlers would display deficits in attending to complex social scenes, especially showing difficulties attending to the speaker's face and mouth (Katarzyna Chawarska et al., 2013; Chita-Tegmark, 2016a). Additionally, I

expect that there would be positive associations between age, eye gaze behaviors, joint attention, and early language development similar to TD counterparts.

Methods

Sample. Data for this study were drawn from the longitudinal Interactive Eye Gaze study (IEGS). The IEGS collected data from the larger Tucson area during the years 2013-2017. The inclusionary criteria for at-risk infants and toddlers included the following: (1) infant siblings of children diagnosed with autism and (2) infants identified with global developmental delays. The infants were excluded if they had pre-existing medical conditions or disorders (i.e. epilepsy, fragile X syndrome, other genetic conditions). The sample included 15 at-risk infants and toddlers from English speaking homes who were recruited between the ages of 3 to 30 months (M = 11.67, SD = 5.73) at visit one. A total of 11 males and 4 females participated in the current study. Table 1.1 displays the demographic information for this sample across the different time points.

Procedure. Informed written consent was obtained from the parents during the initial visit to the lab. Families followed the same procedure for all four visits. All infants participated in a series of standardized developmental assessments by an examiner in order to understand the developmental profiles of these participants (see measures sections below). In addition, parents completed standardized questionnaires regarding their children's adaptive behaviors and language development. Next, the infants were placed in an adjustable high-chair in front of the eye-tracking computer along with their mothers seated next to them, but facing away from the tracker for the presentation of the dynamic stimuli. Each participant's session lasted approximately 90 minutes.

Apparatus and Eye-tracking Paradigm. The Tobii Studio (T60; Tobii Technology, Sweden) eye-tracking model was utilized for this study. This eye-tracking software employs near infrared illumination in order to create the reflection patterns on the cornea and pupil of the eyes of the participant. Advanced image processing algorithms are used to estimate the accurate position of the eye in space and the point of gaze. The T60 eye-tracking model captures data rates at 60 HZ from a 17-inch TFT monitor, situated 65 cm away from the infant. This eye-tracking model allows for a large degree of head movement, with an accuracy of 0.5-1 degree of visual angle. In the current study, scenes from the 1979 version of *The Muppets Movie* (two minutes and 10 seconds) were chosen. The video clip was presented on a 1280 by 1024 pixels screen resolution with built in speakers for audio control. The audio was the original soundtrack from the movie. *The Muppets Movie* depicted a frog (Kermit), a pig (Ms. Piggy), and an adult male (Server) engaged in conversation during dinner. Frames from this stimulus are shown in Figure 1. The dynamic clip featured actors' mutual gaze, averted gaze, and movements towards and away from the camera. The stimulus contained light music in the background that was overlapped by the actors' dialogues in English. The actors spoke approximately the same amount of time with brief silent period in between transitions. This stimulus was chosen primarily because it provided rich visual experiences as well as a range of facial expressions and triadic social interactions.

Eye-Tracking Calibration. While seated in the infant/toddler chair or on the mother's lap, a five-point calibration system was used to establish the individualized eye movements of each infant. The calibration process involved a looming/vanishing blue circle presented on a background of white dots, at each corner of the screen and in the center. At each location, calibration data was collected after consistently hearing three beeping sounds ("dings"). After the

calibration process, the researcher examined a plot of gaze data recorded during the acquisition of each calibration point, eliminating any data points where the infant and toddler was not looking at the target. If enough calibration data was not collected the first time, the infants underwent the same process again.

Measures. *The Early Social-Communication Scales (ESCS)*. The ESCS (Mundy, P., Delgado, C., Block, J., Venezia, M., Hogan, A., & Seibert, 2003) is a filmed 15-20 minute structured observation between the examiner and the child engaged in play. The ESCS observes nonverbal communication in children eight to 30 months of age. The filmed observations were classified by coders into one of three mutually exclusive categories of early social-communication behaviors: Joint Attention Behaviors, Behavioral Requests, and Social Interaction Behaviors. Two independent coders watched all the video recordings of the ESCS in order to determine the frequencies of gestures and nonverbal communication as broken into the three mutually exclusive categories listed above. The coders specifically calculated the frequency of the child's initiating as well as responding behaviors that occurred across joint attention (JA) and behavioral requests (BR). Composite scores for joint attention were created by calculating the initiating and the responding joint attention behaviors (i.e. IJA + RJA). A similar composite score was calculated for BR (IBR + RBR). Finally, the total joint attention scores were calculated by combining the composite JA and BR scores (see Table 2.1). A criterion coder coded 25% of all the videos. The interrater reliability was considered to be sufficient with Cohen's Kappa coefficients of $\kappa = 0.78$ for Joint Attention behaviors, $\kappa = 0.75$ for Behavioral Requests, and $\kappa = 0.76$, for Social Interaction behaviors. A total of four infants were not included for the assessment of joint attention scores due to their ages being outside of the validated assessment age ranges (e.g. ESCS for ages 8 months and older).

The Mullen Scales of Early Learning (MSEL; (Mullen, 1995). The MSEL is a standardized examiner administered developmental measure of language, cognitive, and motor functioning. The MSEL provides age-equivalent and standard scores from birth to 68 months of age. Five subscales were administered and included gross motor, fine motor, visual reception, expressive language, and receptive language. An overall standardized score of intellectual functioning known as the Early Learning Composite was also obtained. Computer calculated age-equivalent standardized scores were used for analysis from the five subscales and summarized in Table 2.1.

Vineland Adaptive Behavior Scales-II (Sparrow et al., 2005). The Vineland-II is a standardized measure for assessing adaptive behavior of individuals from birth to 90 years of age. This measure was administered to the parents by the examiner and assessed four subscales of development including socialization (interpersonal relationships, play and leisure time, and coping skills), communication (receptive, expressive, and written subdomains), motor (fine and gross motor), and daily living skills (personal, domestic, and community subdomains). Standard scores were utilized for the subdomains in order to assess developmental adaptive skills (see Table 2.1).

MacArthur Communicative Development Inventory (CDI; Fenson et al., 1993). The CDI Words & Gestures form is a parent questionnaire that assesses aspects of language development, including gestures, words understood, and words produced by infants and toddlers. The CDI Words and Gestures form (eight to 16 months) assesses the child's responding to name, includes a 396-item vocabulary checklist divided into 19 semantic categories, and rates the child's production of gestures as broken into early (games and routines) and later gestures (actions with objects, imitating adult actions, etc.). The CDI Words and Sentences form (16 to 30 months) was

also utilized for the older toddlers in the study. The Words and Sentences form consists of a checklist of 680 words typically produced by English-speaking children. Additionally, the Words and Phrases section assesses grammar acquisition, whereby parents indicate their child's ability to combine words, provide examples of the three longest sentences, and complete questions related to sentence structures and morphemes the child produces (see Table 2.1). Four infants' initial language assessment was obtained from the MSEL subscale scores due to their ages being outside of the validated age assessment (e.g. CDI measures for administration with ages 8 months and older).

Analytic plan

Eye-tracking Coding and Data Reduction. Raw eye-tracking data outputted from the Tobii Studio software was subsequently analyzed for fixation points using areas of interest (AOIs) in Noldus Observer XT Behavior Software. Independent coders scored frame-by-frame gaze behaviors into one of the seven AOI categories from raw superimposed gaze fixation data files. A total of 182 video clips (3873 frames per participant) were coded for the current study. A fixation was defined as a data point if it remained within a 30-pixel radius for a minimum of 100 milliseconds. The total on-screen area was divided into seven AOIs including: (1) the eye region of the actors; (2) the mouth and chin region; (3) the object region (candle, champagne bottle, etc.); (4) a face region (nose, cheeks, forehead, any area outside of the eyes and mouth); (5) hair; (6) body regions of the actors; and (7) an 'other' region that consisted of any gaze outside of the AOIs. Fixations were also coded for no gaze when the participants looked away from the stimulus displayed on the screen. Coders were trained to 95% agreement before independently coding. Four coders scored the different gaze data and the interobserver reliability as calculated

by the Intraclass Correlation Coefficient (ICC) for the AOI variables Eyes, Mouth, Face, Body, Other, and Objects was 90.6%, 91.4%, 90.2%, 93%, 94.3%, and 91.8%, respectively.

In order to examine differential gaze patterns during dynamic social scenes, the participants' fixation durations (i.e. total viewing time) were calculated. As infants differ in overall fixation duration (FD), proportion of total looking time (PTLT) was calculated for each individual AOI. Dependent variables were based on the amount of gaze on each AOI (eyes, mouth, face, body, hair, object, and other) divided by the total amount of on-screen looking time. Gaze towards the scene was calculated by the total amount of on-screen looking time divided by the scene duration. The scale for the proportions ranged from zero to one. For each child, separate analyses were conducted for the AOI regions of eyes, mouth, and overall scene (i.e. these AOI regions served as dependent variables for longitudinal analyses).

Data from the eye-tracking and developmental questionnaires across the four time points (visit 1 to visit 4) was analyzed using multilevel models (MLM) for longitudinal designs in R 3.2.2 (citation package = nlme) to examine the eye gaze patterns of TD infants and toddlers. These models estimate individual growth trajectories and between-group differences in average levels of the outcome variables as well as trajectories of those variables over time (Singer & Willet, 2003). MLM postulate statistical models at two levels. A level one model depicts each infant's change trajectory (within-person age differences) with growth curve parameters such as the intercept and the slope. Simultaneously, a level two model describes the individual differences in the growth curve as a function of the predictors (between-person differences). As participant data was nested within time, using a MLM approach was beneficial for exploring not only where infants and toddlers began on their gaze and social attention, but also how their growth trajectories changed as development progressed. Thus, time (i.e. each distinct visit)

served as the level-1 predictor and contributors of gaze behaviors were examined as level-2 predictors.

Results

The objective of this study was to evaluate the patterns of longitudinal change in the gaze behaviors of at-risk infants and toddlers during dynamic social scenes from three to 30 months. In addition, the study examined how eye gaze behaviors, joint attention, and language skills would explain the variability among infants' growth trajectories. Multilevel models in a step-wise procedure were used to fit the longitudinal data for the outcome variables of (1) overall PTLT toward scene, (2) gaze towards eyes, and (3) gaze towards mouth. These models were compared with longitudinal developmental assessments of joint attention, expressive and receptive language, and adaptive behaviors.

Descriptive Analyses & Correlational Analyses

Data analysis included descriptive statistics to check for normality, outliers, skewness, and kurtosis. These analyses were exploratory and also included correlations between the predictor and outcome variables. Table 2.1 provides the means and standard deviations for the developmental measures in this study across the four time points. After visually plotting histograms and checking for normality, some primary variables had high skewness and kurtosis values, which resulted in conducting Box-Cox power transformations (Box & Cox, 1964). All primary variables were person-centered for interpretability purposes. More specifically, for the longitudinal analysis of the age and the AOI variables, person-mean centering was applied because an infant's age and AOI gaze scores within his or her age group would be more meaningful than the overall group mean of age or AOI scores. By doing so, we are also able to calculate more accurate estimates for within-group slopes (Bliese, 2006). Table 3.1 provides

correlational analyses between all predictor and outcome variables. Pearson correlation results indicated strong positive relationships between visit (time) and PTLT toward characters' eyes (r = .33, $p < 0.05$), age (r = .48, $p < 0.01$), and the Vineland-II Communication (r = .41, $p < 0.01$), Socialization (r = .34, $p < 0.05$), and Adaptive (r = .32, $p < 0.05$) subscales scores. Additionally, for the AOI data, eyes was negatively correlated with body, (r = -.39, $p < 0.05$) and positively correlated with face, (r = .33, $p < 0.05$). That is, the more time that infants spent on the eyes AOI region, there was a negative association with the amount of time they spent focusing on the characters' bodies. For an assessment of the infants' longitudinal gaze trajectories, a parallel plot of the gaze behavior data as a function of visit is presented in Figures 1.1 and 2.1. Overall, infants' and toddlers' gaze behaviors and the rate of this change varied considerably across visits.

Multilevel Modeling Analyses

To test the developmental predictions, a series of multilevel models were fit for the longitudinal data: First, three unconditional models were fit to examine the variability of eye gaze behaviors between and within participants as well as the mean and variability of the individual growth parameters (i.e. the intercepts and slopes). Second, a series of multilevel models with single level-two predictors were tested. These predictors included total joint attention scores (assessed from the ESCS), Communication, Socialization, and Adaptability scores (measured from the Vineland-II), and Receptive and Expressive language scores, as assessed from the MSEL. Third, the random effect structure of the best multipredictor model: random intercept or random intercept and slope, was tested. Finally, the final model used the most parsimonious random effect structure (random intercept and slope) to test the developmental hypotheses.

Unconditional model for overall scene. The first step of the model development included fitting an unconditional means model (random intercept) and an unconditional growth model (random intercept and slope). The unconditional means model assumes that although infants vary in their gaze behaviors, each individual's developmental trajectory is flat and describes the variation in gaze behaviors. The unconditional growth model assumes that infants differ not only with regard to their initial gaze behaviors, but also with regard to their subsequent growth of gaze patterns. The results from the intraclass correlation coefficient (ICC) indicated that there was 38% variance in the outcome variable of PTLT toward scene that was explained due to differences between infants and toddlers. The fixed effects of the unconditional growth model provided estimates for the intercept and the slope of the population average change trajectory. The results indicated that the estimated average infant displayed 47% decreased attention to overall on-screen looking time with each new visit (level-1 predictor). The visit (time) variable did not significantly predict the infants' and toddlers' changes in overall PTLT toward scene ($p >$ .28). Thus, the next step was to model for no random effect of visit, which meant that an infant's visit was measured without any error (i.e. fixed effect). The results indicated that the model change did improve when visit was predicted as a fixed effect. This was determined by the non-significant likelihood statistic and thus the fixed effect of visit was utilized for further model development. In order to see if an infant's age was a significant predictor of gaze changes over time (level-1 predictor), instead of visit, the unconditional means and growth models were re-run. The results indicated that age did not contribute to changes in the average infant's PTLT toward overall scene ($p > 0.76$). Additionally, visit and age were entered as predictors of infants' overall PTLT and results indicated non-significant results for the main effect of visit ($b = .17$;

$t(25) = 1.71$, $p > .09$) and age ($b = -.03$; $t(25) = -.94$, $p > .35$), as well as the interaction between age and visit ($F(1, 25) = 0.09$, $p > .05$).

Predictor models and model development for overall scene. The second step of the model building included fitting a series of predictor models. To address research question three and whether or not joint attention, language development, and adaptive behaviors influenced gaze behaviors, key predictors were entered into the model. Variables were entered simultaneously as predictors of infant's initial gaze behaviors and their subsequent rate of gaze behavior growth. Results indicated that there was a main effect of visit ($b = .19$; $t(18) = 2.11$, $p < .05$), age ($b = -.06$; $t(18) = -2.13$, $p < .05$), expressive language ($b = .01$; $t(18) = 2.37$, $p = .03$) and receptive language ($b = -.01$; $t(18) = -2.63$, $p = .02$) scores on infants' overall PTLT towards the scene. This meant that the average infant's overall gaze was 58% less with each new visit, when the average infant's age is 15 months, controlling for joint attention, expressive, receptive, and adaptive scores. For language scores, with each new visit, a one-unit change in the infant's overall PTLT, the infant's expressive language scores increased by .01 units. Furthermore, the results indicated that with each new visit while controlling for age, expressive language, adaptive behaviors, and joint attention, a one-unit change in the overall PTLT toward scene was associated with a decrease of 0.01 units in the infant's receptive language scores. Table 4.1 provides the results of the final model with the main effects and the interaction terms. The interaction terms between visit and age at this step were not significant in predicting the infants' and toddlers' changes in gaze behaviors toward overall PTLT for scene. The overall variance in infants' and toddlers' gaze trajectories explained by the final model was 60%. Visual inspection of the residual plots from the final model did not reveal deviations from homoscedasticity or normality.

In order to examine research question two and the specific parts of the face that infants and toddlers focused on, two separate analyses were conducted with gaze toward eyes and gaze toward mouth as the dependent variables as described below.

Unconditional model for gaze towards eyes. Results from the unconditional means and growth model indicated that the intraclass correlation coefficient (ICC) was 21%. This meant that 21% of the variance in the outcome variable of PTLT toward eyes was explained due to differences between infants and toddlers rather than within-person differences. The fixed effects of the unconditional growth model provided estimates for the intercept and the slope of the population average change trajectory. The results demonstrated that the estimated average infant displayed 4% of their gaze toward eyes at visit 1. Visit, a variable of time, did not significantly predict changes in infants' gaze behavior toward eyes (b = .02; $t(27)$ = 1.94, p = .06), but was approaching significance. Building upon the unconditional means model, a model with no random effect of visit was tested. The model with no random effect of time (visit) was more slightly favored in comparison to allowing the time variable to have a random component (i.e. measured with error and comes from a population distribution). Improvements in the model fit were evaluated by comparing fit statistics (-2 log likelihood or -2LL statistic) across nested models of model one and model two (76.12 versus 71.97, respectively). Thus, the subsequent models included no random effect of time (visit).

Predictor models and model development for gaze towards eyes. The second step of the model development included fitting a series of predictor models. Variables were entered as predictors of infant's initial gaze behaviors towards eyes and their subsequent rate of gaze behavior growth. The first predictor entered alongside visit for an infant's gaze behavior toward eyes was age. Results demonstrated no significant effects for age (b = -.00; $t(26)$ = -.84, p = .41)

or visit (b = .03; $t(26)$ = 1.65, p = .11) across time. The next step in the model building process included the main effects of visit, age, and the interaction term for visit and age. Results showed no significance found for the interaction term between age and visit ($F(1, 25)$ = .70, p = .41).

For the final step of the model building, non-significant predictors were dropped and control variables of other AOI regions were added. Specifically, these variables included infants' and toddlers' gaze toward mouth, body, face, objects, and other regions along with age and visit. Results indicated that body (b = -.43; $t(97)$ = -4.18, $p < .01$), face (b = -.38; $t(21)$ = -3.59, $p < .01$), objects (b = -.54; $t(21)$ = -2.68, $p < .05$), and other (b = -.42; $t(21)$ = -3.79, $p < .01$) all significantly predicted children's longitudinal changes in gaze behaviors toward eyes. More specifically, the average infant's gaze toward eyes at visit one when the infant is approximately 15 months old, with average PTLT towards predictors of mouth, body, face, objects, and other was 3%. Additionally, the interaction terms for the significant predictors were entered into the final model and no significant interactions were found. The final model without the interaction terms is provided in Table 5.1. The overall variance in infants' and toddlers' gaze trajectories towards the eyes explained by the final model was 77%. Visual inspection of the residual plots from the final model did not reveal deviations from homoscedasticity or normality.

Developmental assessments & gaze behaviors. In order to examine research question three about how the eye gaze patterns relate to developmental measures of joint attention, language development, and adaptive behaviors, final set of MLM models were conducted. The steps of model building included specifying additional predictors of children's gaze behaviors with visit and age such as total joint attention (TJA), MSEL Composite and the MSEL Receptive and Expressive subscales, and the Vineland-II Socialization and Communication subscales. Thus, the model with visit as the level-1 predictor and age, total joint attention (TJA), MSEL

Receptive and Expressive language subscale, and the Vineland-II Socialization and Communication subscales scores were entered as level-2 predictors for children's PTLT toward eyes. The results indicated non-significant effects for the predictors listed for changes in infants' and toddlers' longitudinal patterns of gaze behaviors toward eyes. That is, the predictors of joint attention, language development, and adaptive behavior did not significantly explain the variation in infants' and toddlers' gaze pattern trajectories toward eyes specifically.

Unconditional model for gaze towards mouth. The next set of MLM analyses included examining children's gaze trajectories and the dependent variable of gaze behaviors toward mouth. The first step of the model development included fitting an unconditional means model (random intercept) and an unconditional growth model (random intercept and slope). The ICC indicated that 3% of the variance in children's gaze trajectories over time towards the actors' mouth was due to between-person differences. The majority of the variance in gaze behaviors toward the mouth can be attributed to within-person differences in the children in this sample. The next step included running the unconditional growth model with visit as a random effect. Results indicated that visit was not significant in explaining the change over time in infants' gaze behaviors towards the characters' mouth ($b = .00$; $t(27) = .50$, $p = .61$). The fit for model one where visit was allowed to vary over time (i.e. random effect) was compared against the fit for a model without random effects. The loglikelihood ratio indicated minimal differences between model with or without the random effect of visit. Based on prior theory, visit was allowed to vary over time and thus modeled as a random effect.

Predictor models and model development for gaze towards mouth. The second step of the model development included fitting a series of predictor models. Variables were entered as predictors of infant's initial gaze behaviors and their subsequent rate of gaze behavior growth

toward the mouth AOI region. Age was the first variable entered into the model and the results demonstrated that neither age (b = .00; $t(26)$ = .31, p = .76) nor visit (b = .00; $t(26)$ = -.05, p = .96) significantly explained the variance in infants' and toddlers' PTLT toward the characters' mouth over time. The next approach for model building included adding in the age and visit interaction term. The results demonstrated a non-significant interaction term ($F(1, 25)$ = .03 p = .86) for visit and age. The final step in the model development included examining which variables specifically were independent predictors of the children's gaze behaviors toward the mouth AOI region over time. The AOI variables of eyes, body, face, objects, and other were incorporated into the model with age and visit. Results indicated that AOI regions of body, face, and other significantly predicted children's changes in gaze behavior patterns towards the actors' mouth. Results from these fitted models are provided in Table 6.1. More specifically, the average infant's gaze toward the characters' mouth at the first visit when the infant is approximately 15 months old, with average PTLT toward predictors of eyes, body, face, objects, and other was 7%. These significant main effects were modeled as interaction terms for the next model building process and no significant interactions were found. The final model was assessed for the variance explained and it indicated that 65% of the variance could be explained in children's gaze patterns toward the mouth over time when AOI predictors, age, and visit were accounted for. Visual inspection of the residual plots from the final model did not reveal deviations from homoscedasticity or normality.

Predictor models for joint attention, language development, and adaptive behaviors for gaze towards mouth. Relevant level-2 predictors were incorporated into the model such as total joint attention (TJA), Vineland-II Socialization, Adaptability, and Communication subscale scores, and the MSEL Receptive and Expressive language scores, along with the age and visit.

Results indicated that the only predictor significantly accounting for the infant's and toddler's gaze behaviors toward mouth was children's joint attention scores, (b = -.00; $t(15)$ = -2.92, p < .01). This meant that a one-unit change in children's gaze behaviors toward mouth over time, controlling for average age and the predictors of adaptive behavior and language skills, the child's joint attention scores decreased by .01 units. Results demonstrated that 15% of the variance could be explained in children's gaze patterns toward the mouth over time when joint attention, language skills, adaptive behaviors, age, and visit were accounted for in the model.

Discussion

The current study aimed to evaluate the eye gaze patterns of infants and toddlers at-risk for ASD starting from age three to 30 months. Additionally, the unique contributions of joint attention, language development, and adaptive behavior skills were also modeled for predicting infants' rate of gaze behavior changes over time. Three key results were found in this current study: (1) the time of the visit, the age, and children's expressive and receptive language skills significantly explained the overall gaze behaviors toward the social scene or PTLT; (2) infants' and toddlers' gaze patterns toward the characters' eyes specifically was predicted by decreases in attention allocated toward body, face, objects, and other; and (3) children's gaze trajectories toward the characters' mouth was predicted by their decreased attention toward body, face, and other. Additionally, over time, the infant's joint attention skills varied their attention allocation toward the mouth AOI region. This study adds to the current literature on social attention and differential gaze allocation by infants at-risk for ASD toward the eyes and mouth regions, an area of study that continues to produce incongruent results (Chita-Tegmark, 2016b; Guillon et al., 2014).

Longitudinal Patterns of Eye Gaze Behaviors: Scene

Research studies focused on understanding the atypical gaze behaviors of infants at-risk for or with ASD have attempted to tease apart the contradictory results found in relations to the attention allocated to social stimuli in comparison to non-social stimuli (Boraston & Blakemore, 2007; Chevallier et al., 2015; Papagiannopoulou et al., 2014). This is important because it provides key developmental perspectives on children with ASD's diminished eye-looking as a source of gaze aversion versus gaze indifference (Klin, Shultz, & Jones, 2015; Moriuchi, Klin, & Jones, 2016). When analyzing infants at-risk for ASD's overall PTLT, results from the current study indicated that the main contributing factors on infants' longitudinal gaze behaviors were the time of the visit, age, and their expressive and receptive language scores. Specifically, the gaze allocated by infants at-risk for ASD toward the social scenes of *The Muppets Movie* was predicted by the age of the infant, the time of the visit, as well as their receptive and expressive language abilities. There has been robust research demonstrating that for typically developing infants, the language abilities improve with age and exposure to social environments, coincided by infants' gaze allocation to the appropriate incoming social cues (Kuhl, 2000; Meltzoff & Kuhl, 2016; Stagg, Linnell, & Heaton, 2014). The current study found similar results with the at-risk sample in that the developmental acquisition of expressive language abilities and age contributed to the differences seen in overall PTLT in infants at-risk for ASD. However, the difference in this study was that the infants at-risk for ASD displayed decreased overall PTLT with each new visit. Similar to previous studies with infants at-risk for ASD, the current study showed a reduced overall attention toward social stimuli when there were many competing audio and visual cues (Chawarska et al., 2013; Chita-Tegmark, 2016b; Guillon et al., 2014). An overall decreased attention to the social scene over the key developmental period of three to 30 months is crucial to tease apart as they posit different target areas of atypical brain function and lend to

different behavioral treatments (Bedford et al., 2014; Pierce, Müller, Ambrose, Allen, & Courchesne, 2001). If children at-risk for or with ASD display atypical gaze behaviors toward social stimuli throughout early development, targeted interventions need to be introduced in order to maintain a developmental pathway that minimally deviates from typical gaze patterns.

Another interpretation for the overall reduced gaze found among the infants at-risk in the current sample could be related to the content of the stimuli itself. For instance, having multiple social characters within the dynamic stimuli could have led to decreased overall attention, as opposed to a busy dynamic scene without any social beings (i.e. moving stimulus of objects, biological motion, geometric patterns, etc.). Prior studies have found increased attention among children with ASD to biological motion and geometric patterns in comparison to dynamic social scenes or images (Chita-Tegmark, 2016b; Guillon et al., 2014; Pierce et al., 2016). Thus, the infants at-risk in the current sample may have displayed atypical and reduced patterns of gaze behaviors to the overall social scene due to the rich nature of triadic interactions as well as socio-emotional cues present in *The Muppets Movie*. The consistent finding of overall decreased gaze toward the social scene over time in the current study speaks to the at-risk infants' overall lack of interest in the social world when competing with non-social stimuli within the environment. For instance, Chevallier and colleagues (2015) found that differences in social attention among individuals with ASD could be attributed to the type of stimuli and whether or not they depict every day interactions. More specifically, the authors found that there were atypical differences in social attention by individuals with ASD, but this was significant only when they viewed dynamic social stimuli depicting interactions (Chevallier et al., 2015). Thus, the diminished attention in general to the social scene could be due to the nature of the interactions between Miss Piggy, Kermit, and the Server.

In general, gaze behaviors have been found to be highly associated with the development of joint attention and language development among typically developing children (Brooks & Meltzoff, 2005; Frischen et al., 2007; Navab et al., 2012). However, an interesting finding from the current study was the difference in how infants at-risk for ASD's expressive and receptive language abilities was associated with the longitudinal gaze patterns to the social scene. More specifically, over time, reduced receptive language scores predicted infants' changes in gaze behaviors to the social scene when controlling for expressive language, age, and time of visit. Over time, at-risk infants' decreased receptive language skills predicted the diminished attention to the overall social scene. In contrast, with each new visit, the at-risk infants' expressive language scores increased on average as the overall attention toward the social scene decreased. The present finding extends some previous longitudinal examinations of early social-communicative behaviors and later language outcomes. Specifically, studies have found that joint attention abilities are often later associated with improvements in expressive language, but not receptive language in children with ASD (Charman et al., 2003; Sigman et al., 1999). Although the present study did not directly test for the at-risk infants' rewarding factor of the social stimulus itself, the differences found in gaze behaviors and language abilities could be attributed to their lack of motivation to engage in social attention in the first place. For instance, unlike their typically developing counterparts, these at-risk infants may not be inherently motivated to participate in social scenes that provide the basis for acquiring and practicing communicative skills through joint attention episodes and communicative bids. Thus, it is critical from an intervention perspective to address the discrepancies found in the contributions of gaze behaviors over time to social scenes between expressive and receptive language. Additionally, the timing of the language acquisition and processing may also dictate the attention allocation by

infants at-risk for ASD who may be operating with different underlying brain mechanisms (Charman, 2014; Dawson et al., 2004; Elsabbagh, Fernandes, et al., 2013).

Longitudinal Patterns of Eye Gaze Behaviors: Eyes & Mouth

In order to assess the different parts of the face that infants and toddlers at-risk for ASD focused on, the current study also analyzed separate longitudinal gaze behaviors for eyes and mouth AOI regions. The results indicated that over time, infants' attention toward the eyes specifically was predicted by their reduced attention to the body, face, objects, and other parts of the scene. Similarly, AOI of body, face, and other regions significantly predicted gaze behaviors toward the mouth over time in infants at-risk for ASD. Results from this study indicated that attention on the mouth AOI did not significantly predict infants' gaze behaviors toward eyes or vice versa, such that more focus on the mouth also explained more focus on the eyes. In general, infants' attention toward other AOI regions highlight the way in which attention is deployed during a dynamic stimulus with visually complex objects and faces. The results from the current study indicated that the infants' overall gaze allocation toward the characters' eyes and mouth was predicted by a reduction in attention toward the body, face, objects, and other. At-risk infants in this sample were also found to be allocating the most attention towards the AOI regions of body, face, and other. This is in corroboration with previous research that shows an increase in attention towards the body in comparison to all other AOI regions during dynamic stimuli presentation (Chita-Tegmark, 2016a; Klin et al., 2002; Shic, Bradshaw, Klin, Scassellati, & Chawarska, 2011). Despite the literature continuing to find incongruent results with differential gaze allocation to the eyes and mouth, the current study adds to the literature on the longitudinal gaze patterns of dynamic social stimuli among infants at-risk for ASD.

In regards to the attention allocated to the mouth AOI, the current study indicated that the majority of gaze differences over time could be attributed to within-person differences to the children in this sample. This is important to note because the factors that influence gaze behaviors during key developmental periods may be strongly affected by how infants in this sample processed the social stimuli in comparison to the population at large. Specifically, by understanding the processing mechanisms at play that allow for developmental specialization of facial recognition and socially relevant stimuli, the impairments in gaze behavior associated with ASD can be addressed as a socially adaptive intervention outcome (Elsabbagh et al., 2014; Moriuchi et al., 2016; Zwaigenbaum, Bauman, Choueiri, Kasari, et al., 2015). The way infants at-risk for ASD extract social information from a given stimuli may differ based on the artifacts of the stimulus itself. For instance, during visually complex social scenes, typically developing individuals increase their attention to faces, especially the eyes and mouth due to the high content knowledge it provides for socio-communicative purposes (Ahtola et al., 2014; Leppänen, 2016; Lewkowicz & Hansen-Tift, 2012; Tenenbaum et al., 2013). However, for infants at-risk for ASD, the atypical social extraction and processing may interrupt attention allocation when the stimulus demands higher recognition. This means that children with ASD may demonstrate overall atypical attentional engagement towards faces, however, this mechanism may be context-dependent (Katarzyna Chawarska et al., 2013; Guillon et al., 2014). With developmental insight into at-risk infants' eye gaze patterns, face processing, and subsequent maturation of the neural circuits, researchers are able to implement eye-tracking research designs that provide more information on this activity-dependent process (Elsabbagh et al., 2012; Jones, Carr, & Klin, 2008).

Eye-gaze behaviors and Joint Attention, Language Development, & Adaptive Behaviors

Alongside understanding children's gaze behaviors during social scenes from an early age, the current study also assessed these relationships with other indicators of social cognition such as joint attention and language. Although in the current study, adaptive behaviors did not significantly predict infant's gaze behaviors towards the overall PTLT for scene, mouth, or eyes; predictors of joint attention and language development provided more corroborating evidence on the influential factors. More specifically, the current study showed that the predictors of joint attention, language development, and adaptive behavior did not significantly explain the variation in infants' and toddlers' gaze pattern trajectories toward eyes. However, gaze behavior changes toward the mouth AOI was significantly predicted by infants' total joint attention scores over time. These results provide crucial information for the underlying simultaneous processes of gaze allocation, joint attention, and language development in infants at-risk for ASD. Deficits in joint attention and language development are among the key predictors of ASD (Murza, Schwartz, Hahs-Vaughn, & Nye, 2016; Zwaigenbaum et al., 2005); thus the differential patterns found in gaze behaviors toward the mouth and the total joint attention scores provide further evidence of these interconnected processes. Early on, if infants at-risk for ASD display reduced gaze behaviors toward the mouth predicted by decreased joint attention scores, as they do in the current sample, this lack of shared visual attention can have cascading effects onto the child's social coordination and engagement skills (Merin et al., 2007; Mundy et al., 2009; Sullivan et al., 2007). This finding of reduced joint attention predicting gaze behaviors toward the mouth over time, while controlling for attention toward other AOIs, highlights the consistent delay found in joint attention skills in infants at-risk for ASD. Specifically, young children with ASD may be frequently missing important socio-communicative cues demonstrated via salient faces, which may be necessary for the development of social engagement with others. Essentially, these

results communicate the importance of providing targeted interventions that specifically focus on joint attention strategies and allocation of gaze and gaze following to appropriate events in the environment. Furthermore, the reduced gaze behavior toward the characters' mouth and joint attention skills provide corroborating evidence for the need to include gaze behaviors as a form of developmental risk factor during screening and early identification of ASD (Barbaro & Halder, 2016; Elsabbagh & Johnson, 2016; Sullivan et al., 2007).

Limitations

The present study has a few limitations that might affect the generalizability of the results. First, the current sample size and the attrition rates were significant factors in this longitudinal analysis. In addition, the sample size was relatively small from which it drew profiles of longitudinal gaze trajectories, which might have reduced the power to detect statistically significant effects. Furthermore, despite having large amounts of eye gaze data, not all at-risk infants completed all four visits. Second, the current sample ranged from the youngest infant being three-months-old to the oldest toddler completing the final visit at 30 months. This presents a wide age range where many developmental processes are being acquired and changes are simultaneously occurring (e.g. language acquisition and production, joint attention, symbolic play behaviors, etc.). Third, the current study utilized only a single measure of social attention (PTLT), as opposed to other gaze measures such as gaze shifting patterns and the number of fixations. However, the PTLT or the fixation duration measure was selected due to its consistent use in the literature. Fourth, the diagnostic status of the infants at-risk for ASD was not evaluated in the current study. That is, the at-risk infants in the current study were not followed until the age of 36 months when a formal diagnosis would generally occur in order to determine the "at-risk" outcome (Lord & Jones, 2012; Newschaffer et al., 2012). Finally, the current sample had a

predominantly White racial group as well as mothers with higher educational degrees. This demographic composition could affect the generalizability across more diverse samples.

Conclusions & Future Directions

The current study is one of the few longitudinal eye-tracking studies that employed an ecologically valid dynamic stimulus in order to examine gaze behaviors from an age as early as three months. Overall, research findings depicting eye-tracking studies in conjunction with event-related potentials (ERPs) have found that at-risk infants later diagnosed with ASD show differences in the perception of social information, visual processing, inflexibility of switching attention, responses to facial stimuli, and sensitivity to eye gaze and gaze following (Ames & Fletcher-Watson, 2010; Boraston & Blakemore, 2007; Elsabbagh et al., 2012; Guillon et al., 2014). However, there continues to be unreliable predictors and behavioral irregularities in the ASD-risk phenotype during infancy (Elsabbagh et al., 2014; Zwaigenbaum et al., 2009). Thus, it is critical to understand the eye gaze trajectories of diverse at-risk infants as a way to inform the emerging atypical patterns related to ASD symptoms. Specifically, it is important to consider not only how the infants' gaze behaviors deviate, but also when they begin to alter. The importance of timing and identifying the atypical patterns early on directly communicates the effectiveness of early intervention (Landa et al., 2007; Ozonoff et al., 2014; Zwaigenbaum, Bryson, & Garon, 2013).

The current study has implications for understanding eye gaze patterns as early as three or six months during the narrow developmental window of opportunity and may provide the necessary early developmental risk indicators for autism. With increased attention to the early identification of autism and BAP characteristics, this study aimed to provide more corroborating evidence of the longitudinal eye gaze "red flags" among at-risk infants and toddlers. One of the

most important contributions for the current study is that it creates a pathway for future research aimed at examining eye gaze trajectories within the context of social stimuli early in infancy. By doing so, this study aims to pave the way for establishing additional phenotypic expressions of gaze behaviors in infants at-risk for ASD that can ultimately inform early identification and diagnostic processes.

Table 1.1

Descriptive information about infants' at-risk at study entry and across longitudinal visits

	Time 1	Time 2	Time 3	Time 4
Age Group (Range)	*N* = 15	*N* = 14	*N* = 8	*N* = 6
3-month-olds (± 1 month)	1	-	-	-
6-month-olds (± 1 month)	2	1	-	-
9-month-olds (± 1 month)	3	2	1	-
12-month-olds (± 1 month)	6	3	1	09
14- to 24-month-olds (9 months)	3	8	6	21
Males: Females	11:4	10:4	7:1	5:1
Child's Race				
Black or African American	1 (6.7%)	1 (7.1%)	1 (12.5%)	1 (16.7%)
White	11 (73.3%)	10 (71.4%)	6 (75.0%)	5 (83.3%)
Mixed/ Other	3 (20.0%)	3 (21.4%)	1 (12.5%)	-
Maternal Education: N (%)				
Less than High School	1 (6.7%)	1 (6.7%)	1 (12.5%)	1 (16.7%)
High School/GED	-	-	-	-
Some College	4 (26.7%)	4 (28.6%)	3 (37.5%)	2 (33.3%)
Associate's Degree	4 (26.7%)	4 (28.6%)	1 (12.5%)	1 (16.7%)
Bachelor's Degree	2 (13.3%)	2 (14.3%)	1 (12.5%)	-
Graduate Degree	3 (20.0%)	3 (21.4%)	2 (25.0%)	2 (33.3%)
Marital Status N (%)				
Single, never married	2 (13.3%)	2 (14.3%)	2 (25.0%)	2 (33.3%)
Married	11 (73.3%)	10 (71.4%)	4 (50.0%)	3 (50.0%)
Divorced	2 (13.3%)	2 (14.3%)	2 (25.0%)	1 (16.7%)

Table 2.1

Means and standard deviations of developmental assessments

Assessment	*Visit 1* *N = 15* *M (SD)*	*Visit 2* *N = 14* *M (SD)*	*Visit 3* *N = 8* *M (SD)*	*Visit 4* *N = 6* *M (SD)*
Age	11.67 (5.73)	14.93 (5.86)	18.38 (6.26)	19.83 (4.75)
Mullen Scales of Early Learning[1]				
Receptive	42.60 (12.90)	39.93 (14.88)	37.13 (11.89)	31.50 (11.55)
Expressive	45.13 (11.10)	45.57 (12.49)	42.25 (15.76)	36.83 (12.89)
Gross Motor	44.67 (11.68)	49.21 (14.64)	42.50 (7.17)	39.00 (10.31)
Fine Motor	44.53 (11.53)	49.36 (15.37)	39.13 (12.79)	36.67 (8.34)
Visual Reception	40.53 (12.50)	43.00 (16.26)	37.50 (15.84)	31.50 (10.17)
Early Learning Composite	87.20 (15.03)	89.50 (24.39)	80.25 (22.56)	71.33 (17.51)
Early Social Communication Scales[2]	*N = 11*	*N = 13*		
Total Joint Attention Scores	42.96 (20.40)	38.69 (19.18)	42.75 (20.81)	42.67 (15.15)
Joint Attention	24.46 (16.68)	20.92 (10.36)	24.69 (14.32)	21.83 (10.38)
Behavioral Requests	18.50 (8.21)	17.77 (9.96)	18.06 (11.72)	20.83 (8.01)
MacArthur Child Development Inventory	*N = 10*[3]*; N = 2*[4]	*N = 9*[3]*; N = 4*[4]	*N = 3*[3]*; N = 5*[4]	*N = 2*[3]*; N = 4*[4]
Words Understood[3]	28.80 (36.29)	47.22 (59.78)	133 (128.95)	91.50 (68.59)
Words Understood Percentile[3]	20.26 (17.45)	26. 04 (29.75)	61.82 (5.88)	27.58 (6.68)
Words Produced[3]	1.60 (1.77)	6.67 (9.75)	53.33 (90.65)	3.50 (2.12)
Words Produced Percentile[3]	44.50 (16.74)	31.06 (31.81)	59.20 (25.10)	26.88 (23.86)
% Total Gestures[3]	28.38 (26.75)	19.70 (24.65)	40.00 (32.79)	22.50 (24.75)
Words Produced Percentile[4]	24.40 (27.44)	15.85 (25.14)	21.80 (19.14)	20.49 (30.42)
Mean Length in morphemes Percentile[4]	13.30 (-)	62.00 (40.78)	38.90 (33.79)	35.50 (43.13)
Vineland Adaptive Behavior Scales-II	*N = 14*			
Communication	90.20 (13.66)	83.29 (13.79)	86.00 (10.74)	69.83 (7.60)
Socialization	95.13 (12.25)	91.00 (9.60)	91.75 (11.89)	81.67 (9.48)
Motor skills	86.79 (14.89)	87.79 (15.43)	85.50 (14.11)	78.00 (6.07)
Daily living skills	97.67 (11.56)	96.00 (12.40)	97.88 (16.91)	85.67 (14.94)
Adaptive skills	90.79 (12.90)	87.57 (12.01)	88.38 (12.69)	76.17 (9.24)

Note. [1]Age equivalent scores. [2]Initiating and responding scores. Total Joint Attention = Composite score of JA + BR. [3]CDI Words & Gestures. [4]CDI Words & Sentences.

Table 3.1

Correlations between all predictor and outcome variables at visit one

Variable	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
1. Visit	-	.48**	.27	.21	.41**	.34*	.32*	.01	.25	.33*	.08	.04	-.04	.05
2. Age		-	.39*	.17	.15	.00	.03	.28	.43**	-.02	-.06	.08	-.11	.32*
3. MSL_RL[1]			-	.83**	.28	.22	.25	.11	-.25	-.21	-.23	.22	-.09	-.31
4. MSL_EL[1]				-	.19	.13	.23	.12	.02	-.22	-.19	.27	-.22	-.19
5. COMM[2]					-	.77**	.89**	.38*	-.08	-.27	.03	.03	.06	-.18
6. SOC[2]						-	.89**	.32	-.17	-.35*	.04	.19	-.02	-.21
7. ADAPB[2]							-	.36*	-.07	-.35*	.12	.17	-.01	-.19
8. TJA[3]								-	.25	-.05	-.37*	.03	.01	-.13
9. Scene									-	.10	-.02	-.21	.19	.06
10. Eyes										-	-.06	-.39*	.33*	-.06
11. Mouth											-	-.04	-.09	.30*
12. Body												-	-.68**	-.07
13. Face													-	-.20
14. Objects														-

Note. [1]Age equivalent MSEL Receptive & Expressive subscale scores. [2]Vineland-II. [3]Initiating and responding Early Social-Communication joint attention scores. Total Joint Attention = Composite score of JA + BR.
*p <0.05. **p <0.01

Table 4.1

Parameter estimates of the fixed effects from the final multilevel model of random intercept and slope models with gaze towards the scene as the outcome variable

Variable			
Fixed effects	*Intercepts*	*SE*	*t-value*
Intercept	-.59*	.43	-1.36
Visit	.20*	.09	1.25
Age	-.06*	.03	-2.13
TJA	.00	.00	1.44
Vin_Adapb	-.00	.00	-.79
Receptive language	-.01**	.01	-2.63
Expressive language	.01*	.00	2.37
Visit * Age	-.00	.01	-.24
Visit * Receptive language	.00	.01	.23
Visit * Expressive language	-.00	.01	-.20

Note. TJA= Total joint attention. Vin_Adapb = Vineland-II Adaptive Behavior subscale.

$*p < 0.05$. $**p < 0.01$.

Table 5.1

Parameter estimates of the fixed effects from the final multilevel model of random intercept and slope models with gaze towards eyes as the outcome variable

Variable			
Fixed effects	*Intercepts*	*SE*	*t-value*
Intercept	.02*	.04	.74
Visit	.02	.02	1.22
Age	-.00	.01	-.88
Mouth	-.21	.21	-.99
Body	-.43***	.10	-4.18
Face	-.38***	.11	-3.59
Objects	-.54*	.20	-2.68
Other	-.42***	.11	-3.79

*$*p < 0.05$. $**p < 0.01$. $***p < 0.001$

Table 6.1

Parameter estimates of fixed effects from the final multilevel model of random intercept and slope models with mouth as the outcome variable

Variable			
Fixed effects	*Intercepts*	*SE*	*t-value*
Intercept	.07*	.03	2.41
Visit	-.01	.01	-.63
Age	.00	.00	.41
Eyes	-.22	.19	-1.18
Body	-.36**	.11	-3.36
Face	-.34**	.10	-3.32
Objects	-.26	.21	-1.23
Other	-.42***	.11	-3.98

**p < 0.05. **p < 0.01. ***p < 0.001*

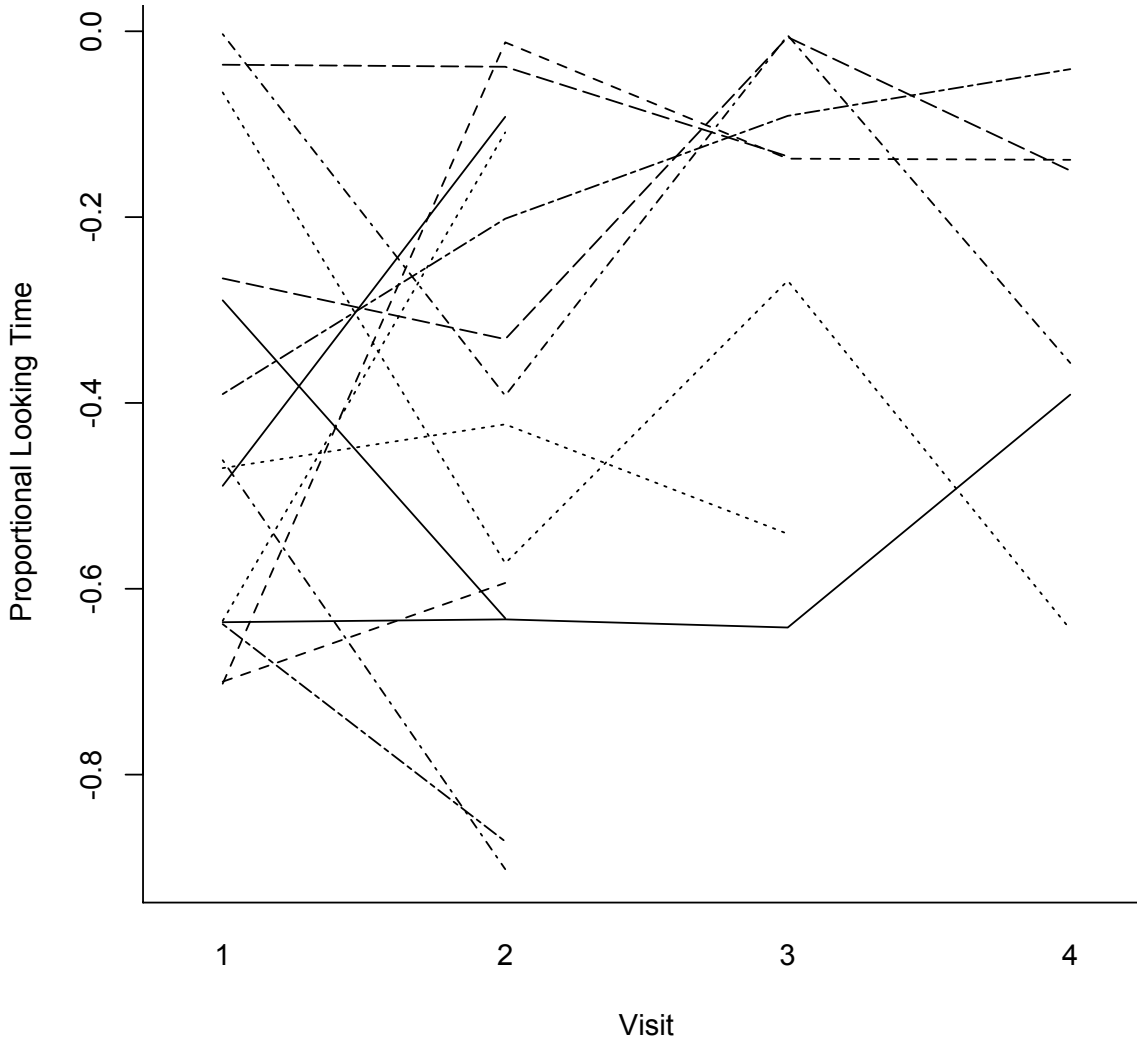

Figure 1.1 Parallel plot of total proportional looking time as a function of infants' visits.

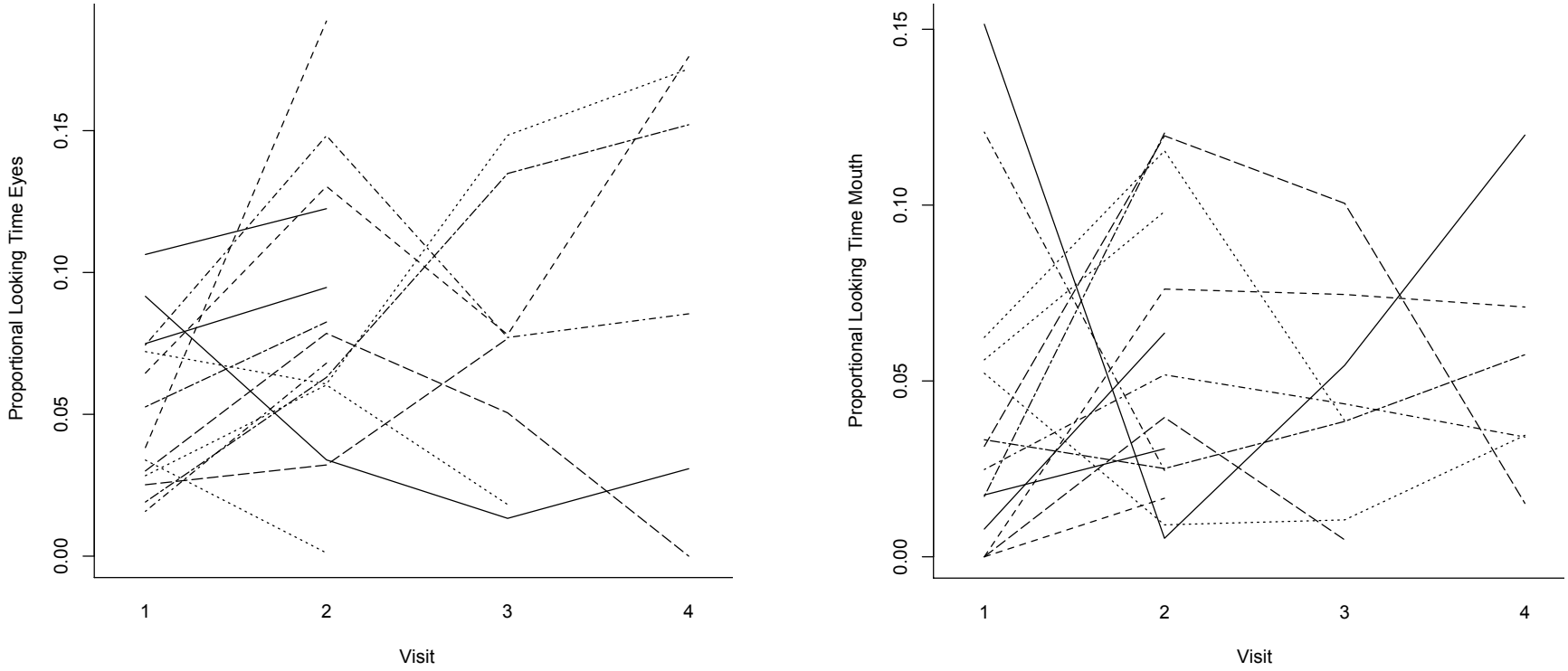

Figure 2.1 Parallel plots of total proportional looking time towards eyes and mouth as a function of infants' visits.

Chapter IV: CHARACTERIZING HEALTH DISPARITIES IN THE AGE OFAUTISM DIAGNOSIS AMONG 8-YEAR-OLD CHILDREN

There are many advantages to having a formal, clinical diagnosis for autism spectrum disorders (ASD) including access to genetic counseling for recurrence risks, intervention and treatment plans, community and public support systems and resources, and the possibility of reducing secondary or co-morbid symptoms through individualized interventions (Caronna, Milunsky, & Tager-Flusberg, 2008; Emerson, Morrell, & Neece, 2016; Johnson & Myers, 2007; S Ozonoff et al., 2011; Zwaigenbaum et al., 2009). Above all, gold standard assessments that provide early ASD diagnostic information for children have proven to be more successful with better overall functioning than the reduced treatment effects for interventions introduced at a later age (Boyd et al., 2010; Zwaigenbaum, Bauman, Choueiri, Fein, et al., 2015).

Research studies conducted on the outcomes of early identification surveyed parents of children already diagnosed with ASD and found that, in most cases, parents often reported having concerns for their child as early as 12 months of age (Barton, Dumont-Mathieu, & Fein, 2012; Crais, Watson, Baranek, & Reznick, 2006; Woods & Wetherby, 2003). While infant sibling research demonstrates the presence of "red flags" of ASD as early as 12 months, and ASD being reliably diagnosed as early as 24 months, many children remain undiagnosed until school-age (Barbaro & Halder, 2016; Johnson & Myers, 2007; Shattuck et al., 2009). This delay between the parents' first concern and the "diagnostic odyssey" is approximately two years with formal diagnosis often occurring at approximately three to four years of age (Barbaro & Dissanayake, 2009; Barton et al., 2012; Daniels & Mandell, 2013; Lord & Jones, 2012). Researchers have previously examined individual, familial, and environmental factors associated with age at ASD diagnosis, with overall trends indicating the age at diagnosis decreasing over

time (Daniels & Mandell, 2013; D. S. Mandell, Listerud, Levy, & Pinto-Martin, 2002). However, this trend has not decreased uniformly for all children, resulting in considerable disparities in the age of ASD diagnoses (Fountain, King, & Bearman, 2011; D. Mandell, Novak, & Zubritsky, 2005; Matson, Nebel-Schwalm, & Matson, 2007).

Theoretical Framework

In order to disentangle the complex effects of unmet health care needs among a specific population, researchers have long used Andersen's Behavioral Model of Health Care Utilization as a theoretical framework for understanding health care needs and services (see Figure 1.2; Andersen, 1995). This model postulates that health care utilization by individuals is a function of three sets of variables: predisposing, enabling, and need. These variables dictate an individual's use of health services and the factors that enable or impede health care use as a result of certain predispositions as well as their need for care. For instance, the first variable of predisposing factors, which include three parameters, dictates how an individual utilizes health services. This includes: a) demographic factors such as age and gender, b) health beliefs, which are attitudes, values, and knowledge people have about health services, and c) social structures such as education, occupation, social networks, and ethnicity, all influence an individual's perceptions of need and use of health services.

In relation to enabling resources that facilitate an individual's choice in health care utilization, community and personal/family factors are also accounted for in the model. These enabling factors include the availability of health personnel and facilities in the area where people live and work as well as having the means to get to those services and make use of them. Specifically, some enabling resources include: income, health insurance, wait times, and travel to secure diagnoses and assessments. According to the Behavioral Model, these enabling factors

directly influence an individual's health care needs and utilization. Finally, the third variable in Andersen's Behavioral model includes need. Need represents judgment about people's functional health status and their need for subsequent medical care as a necessity. In addition, the Behavioral model incorporates feedback loops that show how these outcomes and choices individuals make in regards to their health care needs, in turn, affect subsequent predisposing factors and perceived need for services and health behaviors (Andersen, 1995).

For the purposes of this paper, Andersen's Behavioral model provides a structure for understanding how multiple factors contribute to an individual's risk or resilience status. For instance, when evaluating the delays in the age of ASD diagnosis, predisposing factors such as age, gender, race and ethnicity together can classify an individual's overall impact status (Emerson et al., 2016; D. Mandell et al., 2005). Furthermore, enabling factors such as family income, insurance, and region of residence can directly influence the access to pediatric professionals that can expedite the process of an ASD diagnosis. Finally, need, as captured by the child with autism's functional ability status, could also affect the rate at which an ASD evaluation occurs. For example, if a child with ASD has multiple co-occurring disorders, has a severe form of autism, and has multiple domains affected such as cognitive, adaptive, and social, he or she has more functional health care needs, and is more likely to utilize and need health care services. Furthermore, this theoretical framework demonstrates how the external environment, which are factors not solely related to the child with ASD, also includes parental status and other sociodemographic factors, interacts with the health care system in order to influence a family or child with autism's predisposing, enabling, and need factors for utilizing health services.

Child Factors

Research studies conducted thus far have indicated the importance of understanding the

child's social context and the influence it may have on the timeliness of an ASD diagnosis. For instance, factors such as the child's developmental trajectory, available resources, parental interactions with health services, and educational and financial resources, to name a few, can all impact the process of obtaining a diagnosis for ASD (Bickel, Bridgemohan, Sideridis, & Huntington, 2015; Fountain et al., 2011; Oswald, Haworth, Mackenzie, & Willis, 2015). In general, sociodemographic characteristics have known to play a crucial role in the delayed diagnosis of ASD. However, studies have found conflicting evidence in terms of the effects of racial and ethnic backgrounds and ASD diagnoses. On one hand, studies show that White, non-Hispanic children are diagnosed on average at 5.7 years of age, with African-American and Latino children being diagnosed later at around 6.2 years of age. On the other hand, other studies have found no association of ethnicity on ASD diagnosis (D. Mandell et al., 2005; Mazurek et al., 2014; Rosenberg, Landa, Law, Stuart, & Law, 2011; K. Zuckerman et al., 2013). These inconclusive findings could add to the challenges when efforts to provide earlier diagnoses and prevalence cannot be clearly delineated. Specifically, if diagnostic discrepancies do exist due to racial and ethnic factors, then perceived discrimination on the patient end can also lead to delays in diagnosis due to underutilization of services and/or participation in consultation (Dababnah, Parish, Turner Brown, & Hooper, 2011; Emerson et al., 2016; Shattuck et al., 2009).

Many studies have documented that the type of ASD differentially predicts the age of diagnosis. For instance, Williams and colleagues (2008) found that children in the United Kingdom reported different ages of diagnosis depending on the type of ASD. Specifically, the median age of diagnosis was 44.9 months for autistic disorder and 115.9 months for Asperger syndrome (Williams, Thomas, Sidebotham, & Emond, 2008). This was further corroborated in a review conducted by Daniels and Mandell (2013) whereby over half of the reviewed studies

reported later ages for the diagnosis of Asperger syndrome in comparison to other previous categories of ASDs. Additionally, children who present more severe ASD symptoms, especially language and communication deficits, repetitive motor movements (hand flapping) along with cognitive or intellectual disability, and additional co-occurring diagnoses, are more likely to receive a diagnosis earlier than children with higher functioning ASD and less observable symptoms (Barbaro & Dissanayake, 2009; Bickel et al., 2015; Brett, Warnell, McConachie, & Parr, 2016; Mazurek et al., 2014; McMorris, Cox, Hudson, Liu, & Bebko, 2013; Zwaigenbaum et al., 2009). In a combined model analysis of child and family characteristics by Bickel and colleagues (2015), it was found that for children younger than 36 months, a younger age at diagnosis was associated with child characteristics of higher cognitive functioning, better adaptive functioning, and lower expressive and receptive language abilities (Bickel et al., 2015). In addition, the child's birth order was also found to be a predictor for later births being associated with an earlier age of diagnosis.

In a comprehensive review conducted by Daniels and Mandell (2014), 13 studies reported no association between a child's sex and the age at ASD diagnosis. In one study, Shattuck and colleagues (2009) using data from the Autism and Developmental Disabilities Monitoring Network found that the females in the study were identified as having ASD much later than males at the age of 6.1 years in comparison to 5.6 years for males. An earlier age of diagnosis was also found to be true for the child level factor of developmental regression, which occurs in approximately 20% of the individuals with ASD (Brett et al., 2016; Rosenberg et al., 2011; Shattuck et al., 2009). This developmental regression is usually defined as moderate to severe social and communication skill loss prior to age three as well as a period of typical development that is followed by a loss of acquired skills (Daniels & Mandell, 2013). The

presence of more apparent phenotypic behaviors creates a challenging disparity for children who are in need for services and are more likely to benefit from early intervention, but present less overt symptoms leading to a delay in identification and diagnosis. Therefore, factors beyond clinical presentation need to be evaluated in order to understand the driving forces that delay, mitigate, or expedite the age of ASD diagnosis.

Familial and Environmental Factors

There is a decreasing prevalence of childhood developmental disabilities at increasing levels of SES (Durkin et al., 2010; D. Mandell et al., 2005; D. S. Mandell et al., 2002). However, within ASD, the effect is reversed; several studies have described a higher prevalence associated with higher SES (Daniels & Mandell, 2013; Hrdlicka et al., 2016; Newschaffer et al., 2007; Thomas et al., 2012). In a surveillance-based study conducted by Durkin and colleagues (2010), a trend towards higher ASD prevalence was found with higher SES regardless of factors such as gender, marked regression, a pre-existing diagnosis, and data source (health records versus school records). In addition, children from lower SES backgrounds were likely identified later due to lack of access to diagnostic care and delayed recognition of behaviors (Barbaro & Dissanayake, 2009; D. Mandell et al., 2009, 2005). For instance, irrespective of insured status, families with lower SES had less consistent provider care and reduced coordination between referral services suggested and received (Emerson et al., 2016; Fountain et al., 2011).

In regards to geographic locations and the age of diagnosis, it was found that across parts of the United States, a later ASD diagnosis was associated with living in rural and non-metropolitan settings, with differences seen in access to regional healthcare (Bakian, Bilder, Coon, & McMahon, 2015; Dababnah et al., 2011; Emerson et al., 2016; D. Mandell et al., 2005; Rosenberg et al., 2011). In a study conducted by Kalkbrenner and colleagues (2011), timely

diagnosis of ASD and individual-level geographic access to health services were evaluated. The authors found that of the 206 identified ASD cases, a younger age at diagnosis was associated with proximity to a higher number of specialty physicians such as neurologists and psychiatrists in comparison to areas proximal to early intervention agencies (Kalkbrenner et al., 2011).

Economic barriers, including lower parental education (e.g. no college education) and income are also associated with a later diagnosis of ASD (Goin-Kochel, Mackintosh, & Myers, 2006; D. Mandell et al., 2005; Mazurek et al., 2014; Shattuck et al., 2009). Additionally, in a study conducted by Emerson and colleagues (2016), it was found that being a younger sibling of a child with ASD was associated with an earlier diagnosis, which could be due to the parental familiarity of the warning signs and experience of navigating the healthcare systems (Bickel et al., 2015; Fountain et al., 2011). In addition, Hrdlicka and colleagues (2016) found that an earlier age of diagnosis among 120 children with ASD was correlated with higher parental education as well as age at the time of birth of the affected child (Brett et al., 2016; Hrdlicka et al., 2016). This pattern could potentially highlight the more experienced ability of parents to manage their children's health care needs.

Overall, it is important to consider the demographic and socioeconomic factors listed above as they highlight possible explanations for the current differences seen in prevalence, identification, and diagnosis (Daniels & Mandell, 2013; Shattuck et al., 2009; Zwaigenbaum et al., 2009). Despite all these known independent factors, what is unknown is whether there exist homogenous subgroups of children who, as a group, are more or less likely to experience a delay in ASD diagnosis. Identifying such homogeneous subgroups based on a combination of child, familial, and environmental factors is a first and necessary step in improving our understanding of the relationship between the delays seen in ASD identification and diagnostic outcomes.

Present Study

According to the Centers for Disease Control and Prevention (2016), the state of Arizona has a higher prevalence rate of ASD-one in 66 children in comparison to the national average of one in 68. Although the awareness of ASD across communities has begun to reduce many racial, socioeconomic, and demographic disparities, group differences in the age of ASD diagnosis remain (Emerson et al., 2016; Shattuck et al., 2009). No study thus far has looked into the classification of subgroups of individuals with ASD based on a combination of individual and sociodemographic factors by linking them to diagnostic delays. To better understand the dynamic factors related to ASD diagnostic age, it is important to consider child-level as well as familial- and environmental-level factors. Therefore, with a higher ASD prevalence rate in the state of Arizona, the present paper is guided by two central research questions:

(1) What patterns of sociodemographic and developmental indicators are present among a sample of 8-year-old children diagnosed with ASD in the state of Arizona?

(2) How do these classes relate to the age of ASD diagnosis in terms of the predisposing (e.g. sex), enabling (e.g. median household income) and need resources (e.g. child's intellectual ability)?

Although it is currently known that each factor individually predicts delayed age at ASD diagnosis, what is not known are the particularly meaningful combinations of these factors that are linked more strongly to delayed diagnosis. I expect to describe homogeneous subgroups that face increased health disparities as related to delayed ASD diagnosis among 8-year-old children using a finite number of discrete classes. Through the identification of different groups of children that may be predisposed to or experiencing a distinct cluster of socioeconomic needs,

we can begin to target interventions and policies that effectively reduce the barriers and the health disparities faced by these underserved populations.

Methods

Sample & Population Characteristics. The sample is comprised of data that was collected by the Autism and Developmental Disabilities Monitoring network (ADDM). The ADDM network is a population-based surveillance program established in 2000 by the Centers for Disease Control and Prevention to monitor the prevalence rate of ASD across 11 sites. The current study includes cross-sectional, population surveillance data of 8-year-old children with ASD in the state of Arizona. ADDM staff conducts surveillance in two-phase processes that includes: a) screening and abstracting records, and b) abstracted records are reviewed by trained clinicians to determine ASD case status. The sample includes children that meet the ASD case definition for the study based on the ASD criteria in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR). These children were identified through abstraction of their records available at multiple educational and clinical sources. Trained clinician reviewers scored abstracted data to determine whether ASD case definition was met. The final sample for the state of Arizona included a total number of 4,479 8-year-old children, and subsequently 2,303 children who met ASD case status. These 8-year-old children were born between the years 1992-2002, resulting in surveillance data from the years 2002-2010. ADDM data were subsequently linked to birth certificate and census-tract data to obtain additional familial descriptive measures. Table 1.2 provides the sample population characteristics.

Measures & Procedure. The abstracted data originated from two sources: a) education and b) clinical sources based on the *International Classification of Diseases* (ICD) records.

Specifically, educational records included requesting an electronic listing of all children in special education who were born in the appropriate year and received special education services. Special education records were obtained for all public schools in selected districts within the Maricopa county in the state of Arizona. The variables requested included date of birth, gender, race, language, and special education category or exceptionality (e.g. autism, emotional disturbance, etc.). In addition, health-care or clinical source type data were also abstracted and included the Phoenix Children's hospital, St. Joseph's Hospital Developmental Clinic, Jordan Development Pediatrics, and Cardon Children's Medical Center. These clinical data records were abstracted for variables such as date of birth, greater than a year of service within the system, any recorded list of ICD codes, and demographic variables. Subsequently, children's physical records were reviewed and qualified examiners, including but not limited to, school psychologists, speech pathologists, developmental pediatricians, etc., conducted comprehensive evaluations.

These records were screened for behavioral or diagnostic "triggers" (e.g. child received a documented ASD diagnosis, child had noted loss of skills, etc.). Based on triggers, information from the child's birth through the surveillance year was abstracted into a single composite file for each individual child. Additionally, children's functional skills, including scores on assessments of adaptive behavior and intellectual ability were obtained. Children were classified as having an intellectual disability if they had IQ scores of $\leq$70 on the latest test available within the record. Overall, final abstraction included data entered for variables: (1) address, (2) identifiers, (3) demographics, (4) test results, and (5) description of behaviors that were consistent or contradictory to ASD diagnosis. Finally, the records were matched with birth certificate data as well as census-tract data for additional information on demographic factors.

For instance, race and ethnicity were coded during abstraction of school or clinical sources into categories of white, non-Hispanic; Hispanic, any race; American Indian or Alaska Native, non-Hispanic; Asian or Pacific Islander, non-Hispanic, and Other or mixed race, non-Hispanic. Due to small group sizes in the current sample, categories were collapsed into four: a) white, b) Black, c) Hispanic, and d) Other. When race and ethnicity information wasn't available, Arizona birth certificate data was utilized for missing or discrepant cases.

Census Tract Data. In order to obtain information on the families' geographic and economic factors, raw variables from two outside sources, *U.S. Census Bureau, 2002* and *The American Community Survey* (ACS; U.S. Census Bureau, 2010) were obtained. The U.S. Census Bureau data were collected for each county in the ADDM 2000, 2002, and 2004 surveillance years and for 2006-2010, *The American Community Survey* was utilized to obtain the same census tract variables for children residing in the participating ADDM site and county. *The American Community Survey* (United States Census, 2016) is an ongoing yearly survey that provides information specific to the social and economic needs of a community. The survey collected by the U.S. Census Bureau collects data pertaining to education, housing, jobs, etc.

Variables were pulled for all census tracts and block groups in the participating Maricopa County in Arizona. Analysis variables were then computed to obtain percentage values, but percentile ranking required additional steps, as follows: separate files with tract-level and block-group-level raw data and computed percentages were reproduced to create one file per surveillance year. Tracts and block groups that any site "curtailed" from a surveillance area county in a given surveillance year were then removed from the corresponding data files. Finally, percentile ranks were computed within each site for all analysis variables. The resulting "denominator" files contained socioeconomic status (SES) indicators for all possible census

tracts and block groups within ADDM sites participating in the 2000, 2002, and 2004 surveillance years. Final census data were merged by the CDC staff into six data files, including a file for tract data and another for block group data. For the current sample, three family-level factors were utilized: 1) Median household income, 2) % of families with children under the age of 18 living in poverty, and 3) % of adults with at least high school education completed. In order to merge these variables that were extracted from two different sources (ACS and U.S. Census Bureau) across the surveillance years (2000-2010), descriptive statistics were conducted for initial comparison. Specifically, histograms and deciles were tabulated in order to assess any discrepancies prior to recoding the three listed variables into new merged variables. After rerunning all descriptive analysis and graphs, the merged variable was determined to have minimal discrepancies across the two census sources. This merging of variables allowed for the least amount of missing data across the surveillance years.

Missing data. Despite numerous efforts, it is common in surveillance studies to have some missing data across time. Prior to analysis, data were evaluated for patterns of missingness (i.e., missing completely at random, missing at random) and data were reasonably assumed to be missing at random (MAR). Under MAR, the missing data are related to observed data (i.e. other variables in the dataset), but not to missing data. (Schlomer, Bauman, & Card, 2010). T-test comparisons revealed significant differences between completed and missing data cases, further suggesting that the missing data are MAR and not MCAR (Enders, 2010). The variables of interest for the present analysis had the following missing data patterns: child's recorded race had less than 1.3% of missing data, special education exceptionality in school had 7%, median household income and the proportion of families with children under the age of 18 living in poverty both had 1.8% missing data, and the proportion of the population aged 25 years or older

with at least a high school or GED degree had 1.9% missing data. In order to handle this missing data, Full-Information Maximum Likelihood (FIML) was employed for the indicator variables. This is the preferred method because it makes use of all the available data in order to report parameter estimates without performing listwise deletion (Enders, 2010).

Analytic plan

A Latent Class Analysis (LCA) in Mplus 7.0 (Muthén & Muthén, 1998-2012) was utilized to explore the existence of homogenous classes of 8-year-old children with ASD as associated with their time to diagnosis. LCA is a probabilistic modeling technique that can detect latent (i.e. not directly observable) homogeneous non-overlapping classes that underlie observed data. Through the use of maximum likelihood estimation, LCA has advantages over traditional cluster analysis in that it can define mutually exclusive classes (Lanza & Cooper, 2016). Specifically, this LCA utilized a mixture of continuous and categorical indicators into the model to predict classes that represent characteristics associated with delayed ASD diagnosis. The categorical indicators included: race, special education category, delays seen prior to the age of three in the domains of social, language, and regression skills. The continuous indicators included the proportion of families with children under the age of 18 years living in poverty, the proportion of individuals 25 years or older with at least a high school diploma or GED, and medium household income. The outcome variable was the child's age at first known ASD diagnosis across the surveillance years of 2000-2010.

Model estimation. Latent class models estimate two probabilities: first is the class membership probabilities (i.e. the estimated proportion of individuals in each class), and second is the probabilities of particular responses to indicators given class membership (Lanza & Cooper, 2016). The individual's probability of belonging to a class was calculated as a function

of his or her observed data and the parameter estimates using the maximum likelihood estimator. Class solutions were determined using empirical and conceptual criteria such as the likelihood ratio tests and the information criteria).

Class enumeration. Starting with a 1-class model, there were multiple models that were tested in order to determine the best specification fit to the data as recommendations provided by Masyn (2013). More specifically, the models were allowed to vary in their variance and covariance structures. The number of classes was increased (beginning from one) until the model did not converge or was not well identified. The best fitting model was the one where all the indicator variables were allowed to covary within class, but the variances and covariances were set to be equal across the latent classes. In order to choose the most parsimonious model, absolute fit statistics, relative fit statistics, and classification diagnostics were evaluated.

The absolute fit statistics for categorical data included the likelihood ratio (LR) chi-square goodness-of-fit test and the standardized residuals. The absolute fit statistics compare the model's representation of the data to the actual data (Masyn, 2013). For relative fit statistics, I compared the Bayesian Information Criteria (BIC), Sample Size Adjusted Bayesian Information Criteria (SABIC), Consistent Akaike's Information Criteria (CAIC), the approximate Weight of Evidence Criterion (AWE), the Adjusted-Lo-Mendell-Rubin likelihood Ratio Test (Adj. LMR-LRT), the Bootstrap Likelihood ratio test (BLRT), and the Bayes Factor (BF). Relative fit statistics evaluate the model's representation of the data to another model's representation (Masyn, 2013). For instance, the low relative fit statistics of BIC, SABIC, CAIC would indicate a better model fit given the data. The LMR-LRT and the BLRT tests compare two models (i.e. a model with another model with one less class), and a statistically significant p-value would suggest the model fits the data better than a model with one less class. Finally, BF is a pairwise

comparison of relative fit between two models (i.e. estimated model in favor of another model with one more class), whereby a value of <.10 would indicate evidence in favor of the model with one more class (Masyn, 2013). These relative fit statistics are displayed in Table 2.2

The best fitting model was then evaluated for homogeneity, separation, and classification precision. The classification diagnostics such as entropy, the average posterior class probability (AvePP), the odds of correct classification (OCC), and the modal class assignment proportion (mcaP) were considered. More specifically, these classification diagnostics are estimated based on posterior class probabilities, which are the model-estimated values for an individual's probability of being in each of the latent classes based on the maximum likelihood parameter estimates as well as the individual's observed responses on the indicator variables (Masyn, 2013). Entropy is a summary index of overall precision of classification for the whole sample across all latent classes; whereby values greater than 0.80 are considered high (Masyn, 2013). The AvePP quantifies class-specific measures of how well the set of indicators predict class membership in the sample. AvePP values above 0.70 are considered well separated and adequate (Masyn, 2013). The OCC and the mcaP are both class-specific indexes of specification, within which OCC values greater than 5.00 indicate latent class models with good latent class separation and high accuracy. Table 3.2 provides these classification diagnostics for the five-class solution. As shown, these classes are well differentiated and homogeneous given the mcaP are near the estimated class proportions and within the corresponding 95% bias-corrected bootstrap confidence intervals. Additionally, the AvePP are all greater than 0.70 and the OCC values are all well above 5.0.

Covariates of latent class analysis. In order to further characterize the LCA for relationships between the latent categorical variable and other, observed or explanatory variables

(i.e. auxiliary variables), covariates were analyzed using the statistical method of DE3step and DCAT (Asparouhov & Muthen, 2014). Specifically, different continuous and categorical variables were analyzed in conjunction with the LCA to explore mean and percentage differences across the classes. Mplus utilizes a three-step approach in order to explore the relationships between the LCA and the auxiliary variables. Step one includes estimating the latent class model using only latent class indicator variables. Step two involves the creation of the most likely class variable by using the latent class posterior distribution obtained in step one. The final step involves regressing the most likely class on the predictor variables, accounting for any misclassification that may have occurred in the second step (Asparouhov & Muthén, 2014). The DE3step statistical approach estimates different means, but assumes equal variances for the covariates. The DCAT statistical approach is utilized for categorical distal outcomes and is the preferred method for categorical outcomes. The categorical covariates included child sex, the type of source abstraction (school, clinic, or both), maternal race, and a child with autism's intellectual ability as measured from IQ scores (IQ scores greater than 70 = no intellectual disability and IQ scores less than 70 = intellectual disability). Two continuous covariates included the total number of years of higher education completed by mothers and fathers.

Results

Model fit. Based on the class enumerations, candidate models were compared using their relative fit indices such as BIC, SABIC, CAIC, and the Adj. LMR-LRT to assess whether a four-class or five-class solution was best fitting. A five-class solution was more conceptually parsimonious and meaningful (see Table 2.2).

Description of classes. The interpretation of the final class solutions was based primarily on the model-estimated, class-specific item response probabilities for categorical indicators and

the unstandardized means for continuous indicators. These results are presented in Table 4.2 and depicted graphically in the profile plot in Figures 2.2 and 3.2.

Across time, 8-year-old children with ASD were described based on patterns of endorsing categorical and continuous indicators across the multiple child- and family-level sociodemographic and developmental factors. Class 1 (n = 759; 33%), was the most prevalent class of children identified as ASD case status. A member in Class 1 was likely to be white, not have a special education category in school that was indicative of emotional disturbance, physical impairments, or intellectual disability, and had no known social delays or regression prior to age three. Individuals in Class 1 were also likely to have a high proportion of families with children under the age of 18 living in poverty. In sum, children in Class 1 were likely to be low risk in terms of development, but high risk from a socioeconomic perspective.

Class 2 (n = 512), with an estimated proportion of 22% was characterized by children with known language delays prior to age three. Children in Class 2 were not likely to racially identify as Black or Other, have a special education classification of emotional disturbance, language and learning disabilities, physical impairments, or intellectual disability, or have loss or regression of skills prior to age three. Children in Class 2 were also likely to have a higher proportion of adults aged 25 years or older with at least a high school or GED degree. Finally, children with ASD in Class 2 were less likely to have an autism special education category in school than children in Class 1. In sum, Class 2 was at a medium risk developmentally, but at a low risk socioeconomically.

Class 3 was the least prevalent class, comprised of only 3% of the sample (n = 79). This class was characterized by children with ASD having known language delays prior to age three, but no known regression or loss of skills, and not likely to be members in the Black, Hispanic, or

other racial categories. Additionally, families of children with ASD in Class 3 were likely to have high median household incomes, and this distinguished them from families with children in Classes 1 and 2. In sum, children in Class 3 were at medium risk developmentally, but at a high advantage socioeconomically.

Class 4 had an estimated proportion of 28% (n = 650) and was characterized by a child with ASD likely to be white, non-Hispanic, having a known social and language delay prior to age three, but having no known loss or regression of skills. Children in this class were also likely to have families with a higher proportion of children under the age of 18 living in poverty. In comparison to Class 4 where children with ASD were likely to be white, Class 2 was even more likely to have children who identified as white and Hispanic than any other racial categories. In sum, children in Class 4 were children at high developmental *and* socioeconomic risk.

With an estimated prevalence of 13% (n = 297), Class 5 was mostly characterized by a high proportion of family members aged 25 years or older with at least a high school or GED degree obtained. Children with ASD in Class 5 were also likely to have no known social delay or regression prior to age three. These children in Class 5 were also likely to not have a special education category under emotional disturbance, physical impairments, or intellectual disabilities in comparison to an autism special education classification. A member in Class 1 in comparison to Class 5 was more likely to have no known social or language delays known prior to age three. In comparison to Class 4 versus Class 5, a child with ASD was more likely to report no loss of language than a known loss of language before age three. In sum, Class 5 was at low risk for *both* development and socioeconomic factors.

Covariates of latent class probabilities. Table 5.2 reports the means and standard errors for the continuous covariates as well as the percentages for the different categorical covariates in

relation to the five different latent classes. For instance, when examining the sex covariate, Class 1 had the highest percentage of females in comparison to the other four latent classes. In terms of the abstraction source, Class 2 had the highest percentage of school only records as the available source type and was less likely to have both sources (school and clinic) for a child with ASD. In comparison to Class 5, all four classes were less likely to have both (school and clinic) abstraction data available for their children with ASD. For the covariate of maternal race, after white mothers, Class 1 was most likely to have the highest prevalence of Hispanic mothers. Finally, in terms of child with ASD's intellectual ability, Class 5 had the lowest prevalence of children with ASD who obtained an IQ score below 70 (i.e. having an intellectual disability).

Significant differences were found between Classes 2 and 3 in relation to the father's education. Specifically, Class 3, which was the least prevalent class, had fathers with the highest degree obtained (i.e. completed a graduate degree). Additionally, pertaining to the mother's education, Class 1 in comparison to Classes 3, 4, and 5 had mothers who had completed the least number of years for their education, equivalent to an Associate's or a vocational degree. In sum, for example, Class 1 was the most prevalent class found in the sample (33%) and it had the highest percentage of females; children in this class were less likely to have both school and clinic as the abstraction source; Class 1 had the highest number of Hispanic mothers who had completed the least amount of years for higher education; and fathers who had completed similar years of education by completing either an Associate's or other vocational degrees.

Outcomes associated with latent classes. Finally, I examined the associations between the five latent classes and an outcome variable of the first known age of ASD diagnosis. The age of ASD diagnosis variable was recorded in months and contained an unusually high number of missing cases that failed to impute. Separate outcome analysis conducted between the dummy

coded missing and the non-missing cases resulted in convergence errors for the missing cases. Therefore, only cases with non-missing data (n = 1,234) were included in the analysis for observing relations between a distal outcome (age of first ASD diagnosis) and the five latent classes. In the most recent surveillance study year of 2012, the ADDM data indicated that the median age at the earliest known ASD diagnosis was 50 months across all 11 sites, and 55 months for the state of Arizona (Christensen et al., 2016). For the current sample of 8-year-old children with ASD (n = 1,234), the median age of ASD diagnosis was 59 months. Keeping these national and regional estimates in mind, results showed that Class 3, the least prevalent class (3.40%), had the lowest age of ASD diagnosis (46.74 months) in comparison to Classes 1 (64.99 months), 4 (58.14 months), and 5 (69.78 months). Furthermore, Class 5 had the oldest age recorded for children's first ASD diagnosis (see Table 5.2) in comparison to all other classes.

Discussion

The current study is one of the first to examine the existence of homogeneous classes for the disparities in the age of ASD diagnosis across multiple child and family factors. This person-centered approach elucidates a flexible framework of classes of sociodemographic and developmental factors in 8-year-old children with ASD. Results from the LCA when applied to a heterogeneous disorder such as ASD strongly suggested the likely involvement of several mutually exclusive classes. Thus, empirically and statistically, a five-class solution was supported for the current population-based surveillance study of 8-year-old children with ASD in Arizona.

These findings indicated that for the most prevalent latent class (Class 1; 33%), a majority of children were identified as white. For the family-level factors, Class 1 had a higher proportion of families with children under the age of 18 living in poverty. From the covariates

analysis, results showed that this class was also characterized by the highest percentage of females, mothers with the least number of years of higher education completed after high school, and had the highest prevalence of Hispanic mothers, after white mothers. For the outcome of interest, Class 1's average age of ASD diagnosis was 64.99 months (i.e. ~ five years) in comparison to the national average of 50 months (Christensen et al., 2016). This class pattern is interesting to consider in contrast to individual findings found in the literature. For example, although many studies have found contradictory results regarding the role of race and ethnicity (D. Mandell et al., 2009, 2005; Shattuck et al., 2009), the predominantly white subpopulation found in Class 1 in combination with a higher percentage of these children's mothers identifying as Hispanic could explain the increased age of ASD diagnosis. Previous studies have noted the higher age of ASD identification among Hispanics in comparison to whites (D. Mandell et al., 2009; Shattuck et al., 2009); however, it may not be just the individual predisposing factor of the child's race and ethnicity, but a combination of the child's and the mother's race and ethnicity that contribute to different cultural factors related to ASD identification and diagnosis.

Additionally, Shattuck and colleagues (2009) have also highlighted the differential age of ASD diagnosis among males and females, with females diagnosed on average at a later age. This is similar to the current study's finding of Class 1 having a higher percentage of females as well as a later age of ASD diagnosis in comparison to the national average. However, what is important to note for this latent class is the combination of having a higher proportion of families with children under the age of 18 living in poverty and having the lowest number of years of higher education completed by mothers post high school. These contextual and multi-level family factors are important to consider when applying larger public health policies and allocation of resources. For instance, in order to reduce the age of ASD identification,

interventions introduced at the family level can assist by creating more awareness for the red flags associated with ASD as well as provide support in obtaining more community specific resources for ASD that may not be available otherwise. Specific to Andersen's Behavioral Model, enabling and need resources such as income, health insurance, and access to specialty clinics, all influence the interactions families have with the health care system and the utilization of the different health services.

Results from the LCA indicated a pattern in Class 2 that was distinctive of children with ASD having language delays prior to age three. Children with ASD in Class 2 (22%) were also likely to have a higher proportion of adults aged 25 years or older with at least a high school or GED degree. These results are informative in understanding why the third highest prevalent group of children with ASD also had an age of ASD diagnosis closer to the median age in Arizona (58.93 months and 59 months, respectively). Due to the known variability in when children with ASD are diagnosed, it is important to consider the parental and clinician concerns noted in a child's developmental history. For instance, deficits in the domains of language and communication are often among the earliest reported concerns for parents of children with ASD (Al-Qabandi, Gorter, & Rosenbaum, 2011; Zablotsky et al., 2017). Despite children in Class 2 having language delays prior to age three, it is important to consider other contextual factors that may be contributing to an age of ASD diagnosis that is closer to the median age as opposed to an earlier age. More specifically, a better understanding of the developmental pathway from early concerns to diagnosis is crucial in order to understand its influence on the age of ASD diagnosis. Given that ASD remains mostly a behaviorally defined condition, clarity with case definition and standardized assessments are central to understanding the ASD epidemiology (Newschaffer et al., 2007; Zwaigenbaum et al., 2009). Specifically, although a parent of a child with ASD may

have notable language and communication concerns, the family's interactions with the health care and the education systems prior to obtaining a diagnosis can play an influential role in the age of diagnosis. Therefore, it is not just the noted delays in language that may be dictating the age of diagnosis, but it's the combination of child and family characteristics (Goin-Kochel et al., 2006; D. Mandell et al., 2005).

Even though the current study's results indicated that Class 2 was more likely to have a higher proportion of adults with at least a high school or GED degree, it is important to evaluate the individual number of years completed of higher education by the mothers and fathers. Previous studies have found that higher parental education is associated with an earlier age of ASD diagnosis (Fountain et al., 2011; Goin-Kochel et al., 2006; Robins et al., 2016; Rosenberg et al., 2011; Shattuck et al., 2009). However, by assessing the specific number of years completed of higher education by parents and family members, researchers can obtain a deeper understanding of the family dynamics and how it may contribute to the primary caretaking role of a child with ASD (i.e. hours spent taking care of child's health and therapeutic needs, time away from home, etc.). In addition, the continuous indicator of the proportion of adults aged 25 years or older with at least a high school or GED degree can include additional family members that may or may not be contributing to the household circumstances or directly influencing the child with ASD. Finally, when the categorical covariate of source type was examined with Class 2, this class had the highest percentage of the abstraction source as school only. Studies have found that children who receive their first ASD diagnosis at a non-school setting such as a hospital or specialty clinic were diagnosed at an earlier age than children diagnosed within a school setting (Daniels & Mandell, 2013; Wiggins, Baio, & Rice, 2006). This could help explain

why children in Class 2 were seen to have a later median age of ASD diagnosis, despite having early known language delays and concerns.

One of the most interesting results from the current study includes the patterns found in the least prevalent class (Class 3). With a low prevalence of 3%, children in Class 3 were identified as being at medium risk developmentally due to the children having known language delays prior to age three; yet being at a high advantage socioeconomically because of the highest percentile rank of median household incomes found. When examining this group with the overall median age of ASD diagnosis, children in this class were likely to have the lowest mean age of ASD diagnosis (46.74 months) in comparison to Classes 1, 4, and 5. This finding highlights the potential family-level factors contributing to the age of diagnosis between Classes 2 and 3. More specifically, both Classes 2 and 3 were defined by having children with known language delays prior to age three. As mentioned previously, this is in corroboration of research findings that dictate the presence of more obvious symptoms (i.e. severe cognitive or language deficits, stereotyped motor movements) that may hasten the provision of diagnosis (Shattuck et al., 2009; Zablotsky et al., 2017). However, Class 3 had a lower average age of ASD diagnosis in comparison to Class 2. There may be multiple factors for this age difference. Although Class 3 had known language delays prior to age three, results also showed that this group had a higher number of years completed of higher education by fathers. Specifically, Class 3 had fathers with the highest degree obtained (i.e. completed a graduate degree), which may explain and be highly correlated to the higher percentile rank of median household incomes found in this class. In comparison, Class 2 found a more likelihood of adults aged 25 years or older with at least a high school or GED degree, which can include a range from an Associate's to a Master's level degree. The difference in the educational status of parents and families can again highlight the

importance of understanding the contextual and combination of factors that may be present for these children with ASD obtaining an early or delayed diagnosis. For instance, having a higher median household income may be correlated with an increased amount of resources available for families to address the child's early language delays. As studies have often found in the ASD literature, there is a higher ASD prevalence associated with higher SES (Daniels & Mandell, 2013; Hrdlicka et al., 2016; Newschaffer et al., 2007; Thomas et al., 2012). This would indicate that irrespective of additional factors, families with higher SES are more likely to have consistent interactions with the health care system as well as reduced interruptions in their health care services (Emerson et al., 2016; Fountain et al., 2011; Zablotsky et al., 2017).

Latent Class 4 was characterized by children with ASD who were likely to have delays in not only one domain, but in multiple domains. More specifically, Class 4 had children with ASD who had deficits in *both* social and language skills prior to age three. Having challenges across multiple domains has been found to be associated with an earlier age of ASD diagnosis (Barbaro & Halder, 2016; Daniels & Mandell, 2013; McMorris et al., 2013). For instance, studies have found that greater symptom severity and having more autism-specific symptoms (e.g. repetitive motor movements, lack of verbal and non-verbal communication) has resulted in an earlier age of diagnosis due to the multi-factorial symptomology (D. Mandell et al., 2005; Rosenberg et al., 2011; Wiggins et al., 2006). The results from the current study found that Class 4 had an approximate average age of 58.14 months at the time of ASD diagnosis in comparison to the 50 and 59 months found nationally and locally, respectively. Even though children in Class 4 were likely to be classified as high developmental *and* socioeconomic risk, the lack of an earlier age of ASD diagnosis is important to consider. For instance, an additional challenge that may preclude early ASD identification includes the existence of co-morbid conditions. Specifically, many

young children later diagnosed with ASD have co-occurring conditions such as communication disorders, tuberous sclerosis, fragile X syndrome, and intellectual disabilities, which may potentially mask the ASD signs and risk factors (Boyd et al., 2010; Costanzo et al., 2015; Pierce et al., 2009). Children in this class may be likely to have additional genetic or co-morbid mental health conditions that may not have been noted in their surveillance record or developmental history.

Children with ASD in Class 4 were also more likely to identify as white and Hispanic as well as live in families with a higher proportion of children under the age of 18 living in poverty. This is an important class to acknowledge because having a higher proportion of a socioeconomic disadvantage can be contributory for a delayed diagnosis (Daniels & Mandell, 2013; Newschaffer et al., 2007). More specifically, studies have found that low parental wealth is highly associated with an increased risk of autism (Fountain et al., 2011; Larsson et al., 2005; Shattuck et al., 2009). With reduced access to timely resources, families may experience a greater disparity in managing their children's special health care needs (Durkin et al., 2010; Emerson et al., 2016). Additionally, the process of navigating through the policies surrounding ASD and how best to access the services available from local and state health delivery systems can be an arduous task for the already burdened family. Finally, Class 4 in the current study also found a higher proportion of white and Hispanic children with ASD. Although studies on race and ethnicity and ASD have produced contradictory results, a few studies have found that Hispanic children tend to be diagnosed later than white children (Fountain et al., 2011; Shattuck et al., 2009). The disparity between early identification and diagnosis may also be related to cultural factors that lead to over or under reporting. For instance, depending on the cultural beliefs, some families may have different developmental expectations, which might coincide

with the lack of recognition of delayed symptoms (Barton et al., 2012; Dereu et al., 2012; Shattuck et al., 2009).

Finally, results indicated that Class 5, with an overall prevalence of 13% of the sample was the class with the lowest risk as related to development and socioeconomic factors. Children in this class were likely to have a high proportion of adults with at least a high school or GED degree. Another crucial finding for this class included having the lowest prevalence of children with ASD who obtained an IQ score below 70 (i.e. having an intellectual disability). Additionally, Class 5 had the oldest age recorded for children's first ASD diagnosis (69.78 months) in comparison to all other classes. These results shed an interesting light on the predisposing, enabling, and need resources highlighted by Andersen's Behavioral Model. Specifically, despite children in Class 5 having the lowest developmental risk including intellectual disability as well as minimal familial risk factors, these children had the highest age of ASD diagnosis found. For instance, perhaps the delayed age of ASD diagnosis is related to the families' judgment about their child with ASD's functional health status and their need for subsequent medical care as a necessity. If the child with ASD does not show overt symptoms related to social, language, or other cognitive domains, families may be more likely to delay seeking help for concerns (Shattuck et al., 2009; Zablotsky et al., 2017). Additionally, the results indicating that children in Class 5 were not likely to have an intellectual disability and the associated age of ASD diagnosis is corroborated with previous research studies. For instance, studies with younger and older children with ASD have documented variability in intellectual functioning, often citing IQ as a major contributor of heterogeneity (Landa et al., 2007; Munson et al., 2008). Specifically, the ADDM network study conducted across all 11 sites found that the percentage of children with developmental concerns younger than age 36 months was

significantly higher for children with ASD and concurrent intellectual disability (Christensen et al., 2016). Given that these children were not likely to have an intellectual disability as well as have reduced developmental risks (i.e. unknown social, language, or regression delays prior to age three), the delayed age of ASD diagnosis is better understood. Despite having families with higher educational degrees, children in Class 5 may be more likely to bypass clinical and behavioral standards of assessment if no overt symptoms and developmental histories are readily examined (Barbaro & Dissanayake, 2009; Bickel et al., 2015; Durkin et al., 2010).

Limitations. The current study had a few limitations that may affect the generalizability of the results. First, the study examines cross-sectional data, which albeit are common for large surveillance and prevalence studies, it limits the ability to analyze longitudinal change and patterns. Second, due to certain methodological constraints, the current study only examined one large metropolitan area within Arizona, thus resulting in other urban and rural counties being unaccounted for during abstraction. Third, across the 11 ADDM network sites, there have been single and broad categories of race and ethnicity defined, which eliminate the proportion of individuals identifying by a combination of racial and ethnic identities. Fourth, if a child doesn't have certain developmental, adaptive, or cognitive tests on records, the child's data is evaluated as missing data for the particular variable of interest. Fifth, due to the nature of the ADDM sites conducting large surveillance studies across 11 sites, there exists some measurement error over time and across sites. More specifically, variations in maintaining reliability in data collection and coding methods across sites can introduce potential biases. Sixth, the current study examined ASD as an overall diagnosis rather than assess individual ASD subtypes (i.e. autism, Asperger's syndrome, Pervasive Developmental Disorder, etc.). Finally, there is currently no ongoing assessment or data incorporated on the type of therapies or interventions a child with ASD may

or may not be utilizing post-diagnosis.

Despite these limitations, the present study has many inherent strengths. Many studies thus far have examined the different factors associated with the rising ASD prevalence rates as well as the age of diagnosis; however, the presence of other contextual risks, including but not limited to, the predisposing, enabling, and need factors have not been conclusively addressed (Fountain et al., 2011). The current study was aimed at understanding how a combination of child- and family-level factors can be utilized to identify a subpopulation of homogenous classes in order to improve the current practices in place for early identification and intervention of ASD. Additionally, the ADDM network is one of the largest ongoing population-based surveillance study conducted till date. Finally, utilizing the methodology of a population-based surveillance study discounts the use of convenience sampling or volunteer biases that is often associated with community surveys.

Implications. The findings reported here have considerable clinical and educational importance. These findings have important implications for the timeliness of developmental surveillance, early identification, and early intervention. Obtaining estimates of the timing of ASD diagnosis across mutually exclusive classes that considers multiple child- and family-level factors is fundamental. Specifically, these estimates and known delays in the age of ASD diagnosis can assist with public health initiatives aimed at improving screening and diagnostic practices. Furthermore, this study also highlights the disparities and subpopulations that are at greater risk for late initiation of diagnostic and intervention services. Targeted interventions need to be implemented at a family level rather than for the child with ASD alone. Finally, additional investigation of the underlying behavioral, environmental, and systems-based influences on the

health disparities in ASD prevalence can greatly identify modifiable risk factors that may ultimately improve clinical outcomes.

Conclusions. By using a person-centered approach that classifies children based on holistic risk factors into homogenous subgroups, the gaps between the known "red flags" of ASD and the age of diagnosis can be minimized (Emerson et al., 2016; D. Mandell et al., 2005). Despite increased awareness and resources available for the early identification of children with ASD through eye gaze patterns and clinical observations of reduced joint attention, the average age of diagnosis remains around four years (Barbaro & Dissanayake, 2009; Daniels & Mandell, 2013; Shattuck et al., 2009). Many factors could be contributing to this diagnostic disparity including the age of the child, the severity of the symptoms, co-occurring medical or genetic conditions, sociodemographic characteristics, SES, familial and community factors such as parental interactions with healthcare systems, or geographic barriers (Crais et al., 2006; Dababnah et al., 2011; Ingersoll, 2011; D. Mandell et al., 2009; Pierce et al., 2009).

Future studies should incorporate the screening and diagnostic practices within the communities in Arizona for a more comprehensive representation of factors that facilitate or impede early identification of ASD. Overall, it is important to consider the factors related to disparities in prevalence, identification, and diagnosis that go beyond just the clinical presentation (Daniels & Mandell, 2013; Shattuck et al., 2009; Zwaigenbaum et al., 2009). In addition, disparities in health and age of diagnosis are also important for the advocacy of national and regional policies that promote earlier identification of ASDs (Emerson et al., 2016; D. Mandell et al., 2005; Woods & Wetherby, 2003) for the specific population they serve since healthcare access does not always equate healthcare utilization by all.

Table 1.2

Descriptive statistics of the ASD case status (N = 2303) and their sociodemographic indicators

Variable	*N (%)*
Race	
White	1437 (62.4%)
Black	128 (5.6%)
Hispanic	555 (24.1%)
Other	152 (6.6%)
Special Education	
Autism	1022 (44.4%)
Emotional disturbance	166 (7.2%)
Language and learning disabilities	458 (19.9%)
Physical impairments	128 (5.6%)
Intellectual disability	310 (13.5%)
Other	57 (2.5%)
Social Delay Known Prior to Age 3	
Yes	924 (40.0%)
No	1379 (60.0%)
Language Delay Known Prior to Age 3	
Yes	1823 (79.2%)
No	480 (20.8%)
Regression Known Prior to Age 3	
Yes	341 (14.8%)
No	1962 (85.2%)
	M (SD)
Median Household Income	73.21 (126.16)
Proportion of population age 25+ with at least high school degree or GED	72.38 (129.34)
Proportion of families with children < 18 living in poverty	63.25 (127.06)

Table 2.2

Model relative fit statistics for latent class analysis

Model	*LL*	*npar**	BIC	CAIC	AWE	BLRT *p* (K, K+1)	Adj. LMR-LRT *p-value* (K, K +1)	BF (K, K +1)
Four-class	-30887.71	65	62278.64	62058.97	62407.52	<.001	0.0011	<.10
Five-class	**-30796.82**	**80**	**62212.99**	**61942.622**	**62371.61**	<.001	**<0.01**	**<.10**
Six-class	-30718.84	95	62173.17	61852.10	62361.51	<.001	0.05	<.10

Note. *number of parameters identified.

Table 3.2

Model classification diagnostics for the five-class solution

Class *k*	$\hat{\pi}_k$	95% C.I.*	*mcaP*	*AvePP*	OCC
Class 1	.330	(.238, .336)	.286	.771	6.85
Class 2	.225	(.169, .278)	.211	.778	12.08
Class 3	.034	(.033, .062)	.047	.805	116.23
Class 4	.282	(.262, .362)	.309	.872	17.33
Class 5	.130	(.061, .185)	.146	.770	22.60

Note. *Bias-corrected bootstrap 95% confidence intervals. *mcaP* = modal class assignment proportion. *AvePP* = average posterior class probability. OCC = odds of correct classification.

Table 4.2

Latent Class indicator means, probabilities, and sample sizes

Class Indicators	Class 1 n = 759 (33.0%)	Class 2 n = 518 (22.49%)	Class 3 n = 79 (3.40%)	Class 4 n = 650 (28.22%)	Class 5 n = 297 (12.90%
Median household income[1]	14.44 (5.07)	11.57 (5.07)	98.67 (5.07)	14.67 (5.07)	12.35 (5.07)
Children < 18 living in poverty[1]	74.21 (301.05)	28.85 (301.05)	49.93 (301.05)	74.57 (301.05)	28.18 (301.05)
Age 25+ at least a high school /GED[1]	32.37 (307.27)	72.31 (307.27)	32. 61 (307.27)	32.48 (307.27)	72.34 (307.27)
Race[2]					
White	**0.82***	0.34	0.53	**0.79***	0.40
Hispanic	**0.10***	0.52	**0.30***	**0.10***	0.43
Special education category[2]					
Autism	0.42	0.46	0.34	0.63	0.34
Language & learning disabilities	**0.32***	**0.16***	**0.23***	**0.14***	**0.27***
Social delay[2, 3]	**0.06***	0.61	0.46	**0.75***	**0.02***
Language delay[2, 3]	0.55	**1.00***	**0.82***	**1.00***	0.52
Regression[2, 3]	**0.03***	**0.18***	**0.19***	**0.28***	**0.05***

Note. [1]Continuous indicators with unstandardized means; [2]Categorical indicators with probabilities; [3]Delay known prior to age 3.
*Item probabilities >0.7 or <0.3 are bolded to indicate a high degree of class homogeneity.

Table 5.2

Estimated means, standard errors, and percentages of covariates and outcomes by latent class

Categorical covariates	Class 1: (33.0%) % M (*SE*)	Class 2: (22.49%) % M (*SE*)	Class 3: (3.40%) % M (*SE*)	Class 4: (28.22%) % M (*SE*)	Class 5[b]: (12.90%) % M (*SE*)	Chi-square test of means/probability equivalence
Sex						
Male[a] vs. female	24%	18%	20%	18%	14%	C1 > C4, C5 < C3
Type of abstraction						
Both[a] vs. School	78%	80%	61%	71%	73%	C2 > C5 > C3; C1 > C5; C5 >
Maternal race						
White[a] vs. Hispanic	6%	1%	0%	1%	1.3%	C1 > C2, C3, C4, C5; C5 > C
Child's Intellectual Ability	1.48 (0.03)	1.38 (0.05)	1.41 (0.03)	1.41 (0.03)	1.12 (0.02)	C5 < C1, C2, C3, C4
Continuous covariates						
Maternal education (grades completed)	13.38 (0.84)	16.83 (2.37)	17.23 (1.02)	17.59 (1.60)	16.29 (0.93)	C3, C4, C5 > C1
Paternal education (grades completed)	15.57 (1.43)	14.36 (0.88)	18.52 (1.37)	15.84 (1.29)	17.36 (1.39)	C3 > C2
Distal outcome						
Age in months of ASD diagnosis	64.99 (1.59)	58.93 (2.90)	46.74 (1.41)	58.14 (1.90)	69.78 (1.57)	C5, C1> C3, C4

Note. [a]Reference category or group (e.g. The percentage of females in Class 1 is 24%). [b]Comparison class. OR = Odds ratio. Significant at $p < 0.05$.

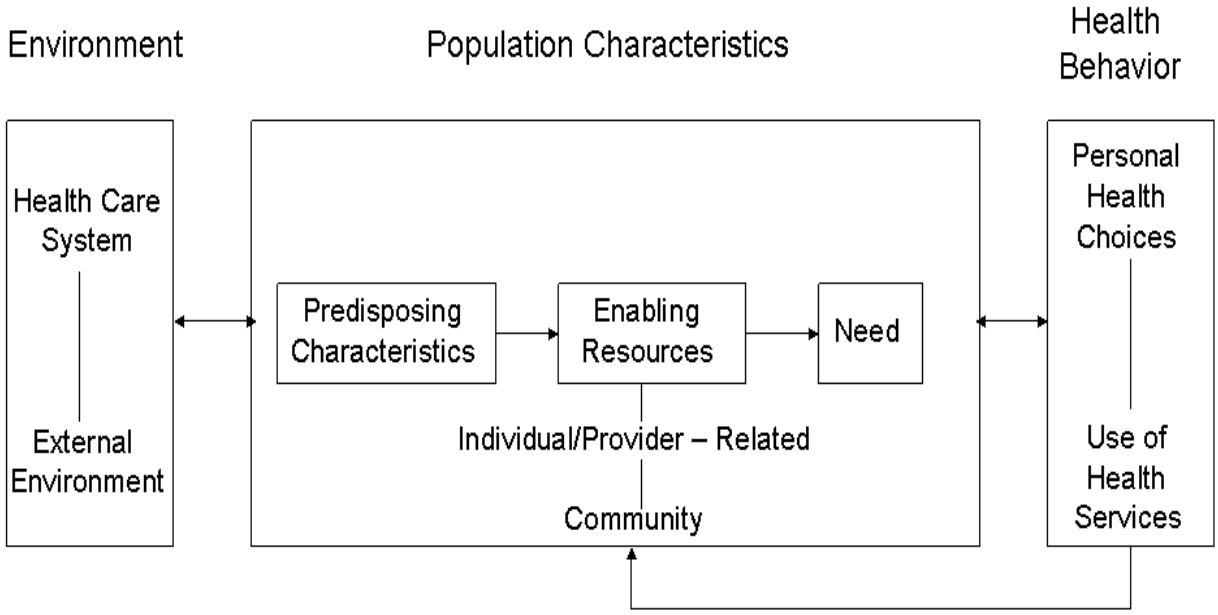

Figure 1.2 Andersen's Behavioral Model of Health Care Utilization

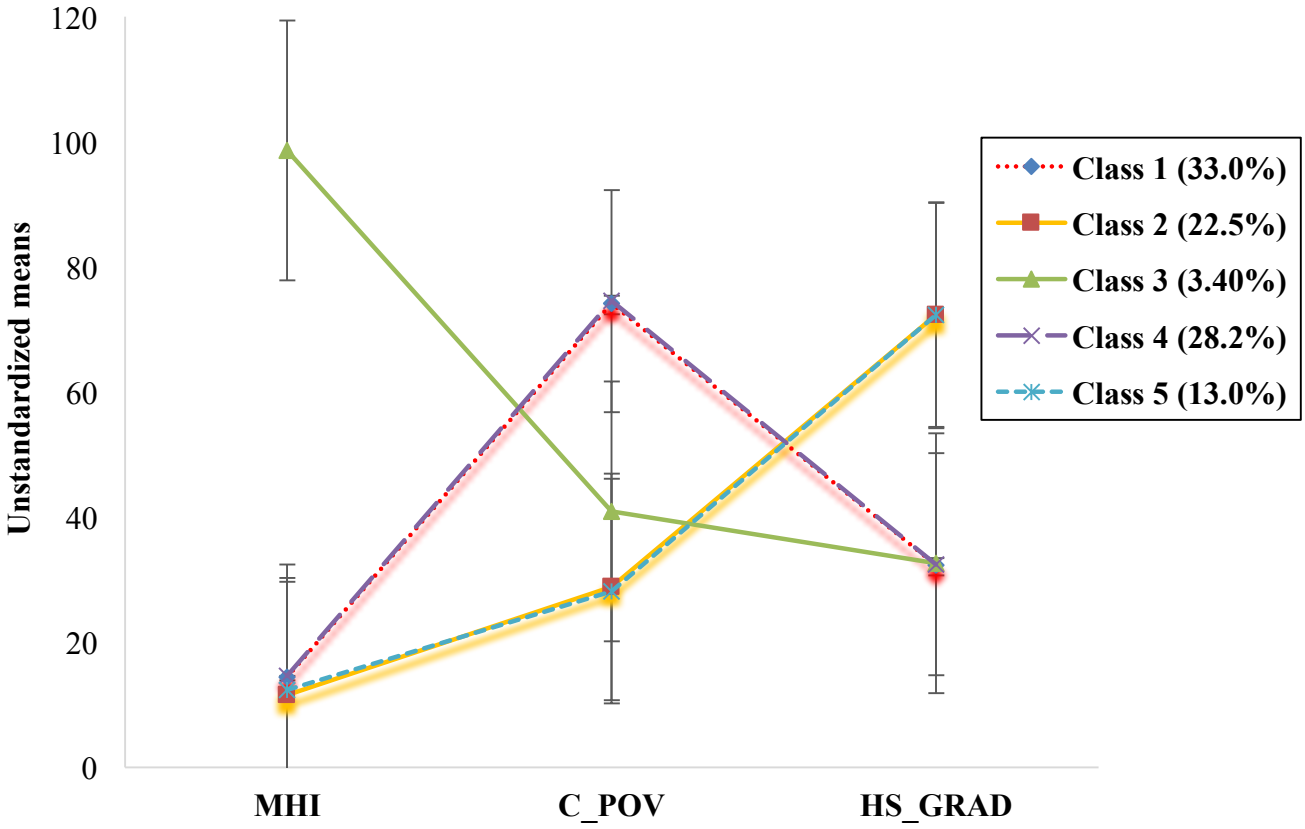

Figure 2.2 Sociodemographic continuous class indicators.

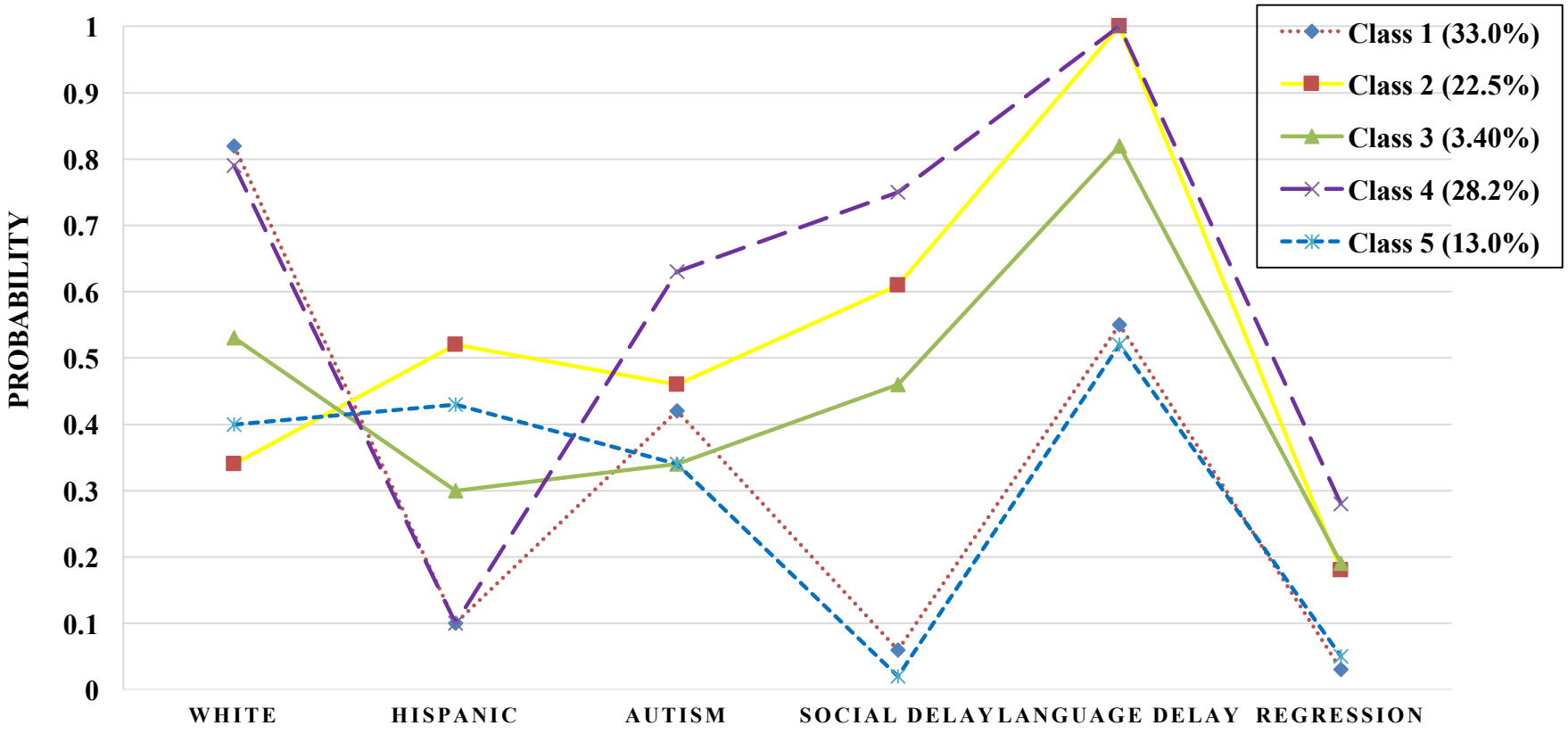

Figure 3.2 Sociodemographic categorical class indicators.

CHAPTER V: CONCLUSIONS

Overview of the three papers

The current dissertation described typically developing and infants at-risk for ASD's longitudinal gaze behaviors within an eye-tracking dynamic paradigm and associations with joint attention, language development, and adaptive skills. Additionally, guided by Andersen's Behavioral model (Andersen, 1995), this dissertation identified an existence of homogeneous classes of individuals that were more or less likely to experience a delay in the age at ASD diagnosis. These three papers, collectively, investigated early patterns of ASD "red flags" and diagnostic processes utilizing advanced analytical and methodological techniques.

The first paper examined the longitudinal gaze patterns of 30 infants and toddlers between the ages of 3-24 months within an eye-tracking paradigm of *The Muppets Movie.* Findings from the longitudinal analyses indicated that overall proportional total looking time was not significantly influenced by an infant's age or the time of visit. In addition, the key predictors of developmental measures such as joint attention and language development also did not contribute to gaze trajectory changes for overall PTLT toward scene. However, when further examined, overall visit or time did influence infants' gaze behaviors toward eyes and mouth above and beyond gaze allocation to other AOI regions. More specifically, there were differences in the ways infants viewed the AOI regions of eyes and mouth, as well as gaze differences between the social actors over time. Results highlighted the importance of measuring longitudinal gaze trajectories in TD infants to establish a comparison basis for high-risk infant groups. Conclusions drawn from this paper shed light on the contextual characteristics for understanding the gaze behaviors that may exist early on during development, and it's relations to developmental measures of joint attention, language development, and adaptive behaviors.

The second paper utilized the same methodology and analytic tools from paper one and examined the prospective gaze behaviors of 15 infants at-risk for ASD based on their genetic linkage to an older sibling previously diagnosed with ASD. Results from the second paper demonstrated that the time of the visit, age, and children's expressive and receptive language skills significantly explained their overall gaze behaviors toward the social scene. In addition, infants' and toddlers' gaze patterns toward the characters' eyes and mouth specifically were predicted by decreases in attention allocated toward other AOI regions such as body, face, and objects. Finally, over time, the infant's joint attention skills varied with their attention allocation toward the mouth AOI region, but not the eyes. Findings from the current paper highlight the diverse gaze patterns by infants at-risk for ASD toward the eyes and mouth regions, an area of study that continues to produce incongruent results. Conclusions drawn from this paper highlight the importance of timing and identifying contextual factors for not only *how* the infants' gaze behaviors deviate from expected gaze patterns, but also *when* these altered patterns begin to appear.

The third paper was one of the first studies to utilize a person-centered approach to examine the existence of homogeneous classes among 8-year-old children with ASD in Arizona that faced disparities in the age of ASD diagnosis. Results from the latent class analysis indicated that interactions between several sociodemographic and developmental factors contributed to the existence of five mutually exclusive classes. Across the surveillance years of 2000 to 2010, 8-year-old children with ASD were described based on patterns of endorsing categorical and continuous indicators across the multiple child- and family-level sociodemographic and developmental factors. Results demonstrated that children in Class 1 were likely to be low risk in terms of development, but high risk from a socioeconomic perspective. Class 2 was at a medium

risk developmentally, but at a low risk socioeconomically. Children in Class 3 were at medium risk developmentally, but at a high advantage socioeconomically. Furthermore, children in this class also had the lowest age at ASD diagnosis. Class 4 children were at high developmental *and* socioeconomic risk. Finally, Class 5 was at low risk for *both* development and socioeconomic factors, and had the oldest age recorded for children's first ASD diagnosis in comparison to all other classes. Findings from the current paper highlighted the gaps that existed between the early detection of ASD and the subsequent age at diagnosis.

Implications and future directions

Known to be a complex disorder with a strong genetic basis, ASD develops within the first three years of life with a diagnosis occurring on average at approximately four to five years of age (Jones, Carr, & Klin, 2008, Newschaffer et al., 2007). Developmental screening tools used in clinical practice through parent reports and physician observations have the ability to detect children at-risk for ASD as early as 18 months of age, but even earlier and more reliable systematic detection is imperative (Dawson et al., 2010; Ozonoff et al., 2011; Rogers, 2009). In addition, with neural pathways becoming established during the first two years of life, identification of atypical behaviors during this critical window can lead to earlier intervention services, providing the most effective chance of minimizing the ASD-related deficits (Elsabbagh & Johnson, 2010; Rogers, 2009).

Despite these known advantages, there is a lack of overt, standardized behavioral markers within the first 12 months that could mitigate the course and timing of the expression of symptoms (Elsabbagh et al., 2012; Pierce et al., 2015; Rogers, 2009). For instance, studies have been able to show that previously known secondary symptoms such as irritability, anxiety, poor gross motor development, and responsivity can appear well before the behavioral symptoms

related to social-communication deficits (Bryson et al., 2007; Landa, Holman, & Garrett-Mayer, 2007; Ozonoff, Heung, Byrd, Hansen, & Hertz-Picciotto, 2008; Rogers, 2009). The investigation of these early risk markers is important for identifying behaviors that are simple analogues to later occurring autism as well as how these behaviors can reduce the child's social and cognitive learning opportunities (Ames & Fletcher-Watson, 2010; Zwaigenbaum et al., 2005). Through eye-tracking paradigms, researchers can explore and highlight the underlying neural networks that are associated with atypical gaze behaviors to describe early red flag behaviors, prior to the age of diagnosis (Klin, 2008; Tager-Flusberg, 2010).

Future studies need to incorporate more randomized control trials for intervention purposes in order to consider the highly variable nature of ASD across different individuals to further move the research field to the most meaningful and clinically significant outcomes (Barbaro & Dissanayake, 2009; Boyd et al., 2010; Damiano, Mazefsky, White, & Dichter, 2014). Prospective and longitudinal study designs will also help researchers understand the developmental and heterogeneous nature of ASD as well as the timing of specific triggers (Damiano et al., 2014; Lord & Jones, 2012; Zwaigenbaum, Bauman, Stone, et al., 2015). Finally, research efforts need to be better integrated with national and state policies in order to provide the most coordinated service delivery system for those highly vulnerable individuals in need of services (Mandell et al., 2009; Pierce et al., 2009; Zuckerman et al., 2013). For instance, by incorporating universal standards of developmental surveillance and screening practices across well-child visits, as recommended by the American Academy of Pediatrics, early identification practices of ASD can be understood and targeted in order to assist with timelier intervention services.

Research devoted specifically to the identification of ASD biomarkers can provide

further clues about the phenotypic expression of ASD (Fakhoury, 2015; Ingersoll, 2011). Despite ongoing large-scale studies, there is tremendous heterogeneity within the phenotypic expression of genetic risk factors in ASD contributing to the paucity of genetic variants identified for the purposes of clinical use (Fakhoury, 2015; Ingersoll, 2011; Walsh, Elsabbagh, Bolton, & Singh, 2011). Given the implications of timing of the diagnosis and issues of dosage for early intervention practices, these eye-tracking paradigms can provide evidence for red flags at key developmental ages, which can further benefit both primary care providers and parents to establish awareness surrounding ASD risk factors (Johnson & Myers, 2007; Zwaigenbaum et al., 2005). With ASD increasing in prevalence and with the associated lifetime costs for supporting a person with ASD estimated to be $2.4 million; identification of red flags associated with ASD need to occur earlier in life rather than later when untreated deficits become more prominent (Baxter et al., 2015; Dababnah et al., 2011; Emerson et al., 2015; Koegel et al., 2014). Certainly, understanding TD eye gaze patterns allows comparisons for deviations in high-risk infants' gaze behaviors and social attention trajectories. Thus, early intervention prior to the emergence of secondary behavioral issues can greatly mitigate adverse developmental trajectories, the clinical course, and the subsequent quality of life for young children at-risk for or with ASD.

Summary

The aim of the three papers in the current dissertation study was to analyze longitudinal gaze patterns and disparities in the age of ASD diagnosis in order to inform research on endophenotypic markers and the early identification and diagnosis of ASD. Findings indicated important red flags related to gaze behaviors and the combination of sociodemographic and developmental factors that may aide future research on minimizing the gap between early concerns for ASD and obtaining a clinical diagnosis. Furthermore, research utilizing a

prospective design allows one to test different hypotheses and identify behavioral markers of ASD both within and across groups, while simultaneously accounting for longitudinal changes. Although ASD is a heterogeneous disorder with a complex interaction of strengths and weaknesses, efforts for earlier identification need to continue evolving in order to tailor early intervention services that provide the most meaningful results and longitudinal outcomes related to social engagement.

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