Utility of Social Attention Eye-Tracking Measures as Predictors of Response to Intervention

Sandy Trinh

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Janine Jones, Chair

Mendy Minjarez

Elizabeth Sanders

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Abstract

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Sandy Trinh

Chair of the Supervisory Committee:

Janine Jones

Department of School Psychology

Early interventions for children with autism spectrum disorder (ASD) are variability effective, and examination of child characteristics of as predictors of response to intervention have been limited. Based on the social motivation theory, reduced basic visual social attention and joint attention behavior are downstream indicators of reward processing deficits. As such, these measures of social attention may predict child responsiveness to interventions relying heavily on reward learning strategies. Eye-tracking measures of social attention may be particularly useful predictors given their efficiency, high resolution, and ease of administration. However, their properties and construct validity have not been sufficiently investigated. In this study, I examined the properties and construct validity of social attention eye-tracking measures to determine their potential utility as predictors of response to intervention. Differences were not

found between ASD and typically developing control groups on percentage of time spent looking at social scenes on a preferential looking eye-tracking task, or on accurate gaze shifts in a response to joint attention eye-tracking task. Age effects may have mitigated group differences. However, participants with ASD had more gaze transitions between face and target object in an initiation of joint attention eye-tracking task. Examination of the eye-tracking measures with more ecological behavioral measures revealed preliminary construct validity for the basic visual social attention eye-tracking task but not for the joint attention eye-tracking tasks. These findings indicate that the eye-tracking measure of basic visual social attention holds promise as a predictor of response to intervention and suggest a need to examine this measure as a pre-test variable in future studies of intervention effectiveness.

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CHAPTER 1: INTRODUCTION

Autism spectrum disorder (ASD) is a neurodevelopmental disorder affecting approximately one in 54 individuals in the United States (Maenner, Shaw, & Baio, 2020). Characteristic social communication challenges and repetitive and restricted behaviors and interests emerge within the first years of life (American Psychiatric Association, 2013), and early intensive behavioral and developmental interventions have shown evidence of effectiveness in producing long-term improvements in cognitive, language, and adaptive functioning (Sandbank et al., 2020). However, not all individuals appear to benefit equally from any given intervention (Howlin, Magiati, & Charman, 2009; Landa, 2018). For example, an examination of 100 toddlers with suspected ASD found 17% showed limited gains over time despite receiving early intensive behavioral intervention (Kim, Macari, Koller, & Chawarska, 2016). Still unclear are factors related to this variability in effectiveness and how to individualize interventions to optimize outcomes (Reichow, Hume, Barton, & Boyd, 2018; Stahmer, Schreibman, & Cunningham, 2011; Vivanti, Prior, Williams, & Dissanayake, 2014; Zachor & Ben-Itzchak, 2017).

Understanding how to efficiently individualize interventions for children with ASD is particularly crucial for several reasons. First, the most critical period of development of the human brain occurs within the first years of life, during which the vast majority of neuronal and synaptic growth and refinement occur (M. H. Johnson & de Haan, 2015). Intervening effectively as early as possible during development is, therefore, believed to result in optimal outcomes (Zwaigenbaum et al., 2015). Second, a scarcity of resources results in long waiting times to receive intervention services (Downs & Downs, 2010). Poor understanding of how to best individualize interventions results in a trial-and-error method of intervention matching, creating inefficiencies in utilizing already scarce resources. Given the significant impact of poorly

matched interventions, developing efficient and effective predictors is paramount to achieving optimal outcomes for all children with ASD.

Early Interventions for ASD

The best predictors are theoretically determined by factors related to both characteristics of the interventions and characteristics of individuals with ASD (Vivanti, Prior, et al., 2014). One should consider the scientific foundations upon which interventions are developed. What is the approach of a particular intervention in improving a child's outcomes? What child characteristics does the intervention leverage to improve functional skills? Interventions with some evidence of effectiveness developed thus far rely broadly on theoretical foundations of behaviorism and developmental science (Sandbank et al., 2020). In the 1960s, applied behavior analysis (ABA), an approach to behavior change grounded in behaviorism, gained popularity and is now one of the most recommended treatment methods for individuals with ASD (Dawson & Bernier, 2013). Behaviorism rests on the idea that behaviors are a result of classical conditioning, the pairing of a stimulus that evokes a response with a neutral stimulus such that the neutral stimulus eventually evokes the same response, and operant conditioning, a method of learning through rewards and punishment (Cooper, Heron, & Heward, 2007). Many early interventions for individuals with ASD are grounded in behaviorism and rely on ABA principles to varying degrees. Discrete trial training (DTT) relies exclusively on behaviorism and utilizes the concept of operant conditioning in a structured, discrete format. An individual's behavior is shaped by manipulating the antecedents and consequences of behavior. The use of rewards as a consequence following desired behavior is commonly used to teach new skills. It follows that the more difficult it is to find a rewarding consequence, the less effective an intervention based on

operant conditioning may be. Predictors of response to intervention should, then, account for motivational factors, such as interest in or attention to objects or people.

Research in developmental sciences in the 1980s and 1990s catalyzed a shift toward incorporating evidence of early developmental learning processes into intervention methods (Schreibman et al., 2015). Several important ideas based on developmental science were incorporated. First, the social relationship and affective exchange between adult and child is paramount to learning (Rogers & Pennington, 1991). Interventions should be delivered in a "naturalistic" and socially interactive environment using child-directed activities. Second, precursor skills are crucial to learning more complex skills, such as acquiring joint attention before language (Mundy, Sigman, & Kasari, 1990). Children with autism demonstrate developmental paths similarly to typically developing children in various domains; that is, they follow regular developmental sequences. Finally, children are active "hypothesis-testers" (Saffran, Aslin, & Newport, 1996). Children learn best when presented with concepts just beyond their current ability (i.e., zone of proximal development). Strategies should be used that actively engage a child's attention and help the child build connections from existing knowledge to new experiences to help them figure out the world around them. Interventions such as Floortime/DIR (Developmental, Individual Differences, Relationship-based) draw primarily on these developmental principles. More recently, a class of interventions, termed Naturalistic Developmental Behavioral Interventions (NDBI), has incorporated both behavioral and developmental principles (Bruinsma, Minjarez, Schreibman, & Stahmer, 2020). While NDBIs have many similarities, differences lie in developmental focus and utility of operant conditioning. For instance, Joint Attention, Symbolic Play and Engagement Regulation (JASPER) is a targeted intervention that focuses primarily on the earliest developmental skills

within social communication, namely engagement and joint attention. Operant conditioning is utilized but to a lesser degree than in other NDBIs or purely behavioral interventions. Pivotal Response Training (PRT) utilizes a naturalistic context but embeds contingency-based trials with greater frequency than other NDBIs. Even within the most comprehensively "packaged" NDBIs (e.g., Early Start Denver Model or ESDM), effective predictors may aid in more efficiently individualizing interventions.

Consideration of predictors of response to intervention should account for theoretical differences in learning employed in the various interventions. For example, the extent to which an intervention based on operant conditioning is effective may be dependent on a child's reward processing development. In addition, precision with understanding a child's developmental level in social communication may lead to efficient referrals to interventions targeted to a child's particular zone of proximal development or, for more comprehensive packages, to more quickly determine appropriate treatment goals and effective strategies for each child. In addition to accounting for theoretical foundations of interventions, understanding child characteristics may further our ability to narrow down predictors of response to intervention.

Characteristics of ASD

By definition, all individuals with ASD have a number of behavioral characteristics. *DSM-5* diagnostic criteria for ASD consist of symptoms within two broad domains: social communication impairments and restricted and/or repetitive interests and behaviors (American Psychiatric Association, 2013). Within the social communication domain, individuals with ASD show impairments in each of three symptoms areas: 1) socio-emotional reciprocity; 2) nonverbal social communication; and 3) social relationships. Socio-emotional reciprocity refers to the back and forth nature of social interactions. Deficits in this area may include difficulty with initiating

social interactions, responding to others' attempts at social interactions, maintaining back-and-forth conversations, sharing interests, emotions, or affect with others, and offering comfort to others. Deficits in nonverbal communicative behaviors used for social interaction include poor or inconsistent eye contact, poorly integrated verbal and nonverbal communication, limited range of facial expressions and gestures, poor body language, and difficulty understanding the nonverbal cues of others. Finally, individuals with ASD have difficulties developing, maintaining, and understanding social relationships. This may manifest in difficulty sharing imaginative play, a lack of interest in peers, difficulty adjusting behaviors to suit different situations, and difficulty developing or maintaining friendships.

In the domain of repetitive and restricted behaviors and interests, individuals with ASD present with behaviors in at least two of four areas (American Psychiatric Association, 2013). The first is stereotyped or repetitive speech, motor movements, or use of objects (American Psychiatric Association, 2013). Speech of this nature includes echolalia or idiosyncratic phrases. Motor movements may include hand flapping, finger flicking, or repetitive spinning or bouncing. Repetitive use of objects may include lining up toys or repeatedly dropping them from the same distance. The second area is restricted interests or unusual preoccupations (American Psychiatric Association, 2013). An individual with ASD may have interests abnormal in intensity or preoccupations with unusual objects, such as street signs or toilets. The third area is rigidity in routine or personal environment (American Psychiatric Association, 2013). This may include extreme distress at small changes, difficulty transitioning, rigid thinking patterns, greeting rituals, or the need to eat the same food or take the same route every day. The final area includes hypo- or hyper-reactions to sensory input or an unusual interest in sensory aspects of the environment (American Psychiatric Association, 2013). Examples of these include an apparent

indifference to pain or temperature, aversion to specific sounds or textures, excessive smelling or touching of objects, or visual fascination with lights or movement.

Additionally, symptoms must be present in early development, usually within the first three years of life, although they may not become fully manifested until social demands exceed limited capacity, and symptoms may be masked by learned strategies later in life (American Psychiatric Association, 2013). Symptoms must also have a significant impact on adaptive functioning and are not better explained by intellectual disability or global developmental delay.

While all individuals diagnosed with ASD meet the above criteria, the etiology and phenotype of autism remain complex and varied among individuals, and difficulty parsing this heterogeneity has contributed to continued difficulty effectively individualizing interventions.

Heterogeneity in ASD

Observations of phenotypic heterogeneity in ASD have been reported since 1943 when child psychiatrist Leo Kanner described a group of children with "extreme autism, obsessiveness, stereotypy, and echolalia" (Kanner, 1943), while German psychiatrist Hans Asperger described a group of patients he termed "little professors," who exhibited similar but more mild social communication difficulties and had a tendency to explain topics in great detail (Asperger, 1944). Attempts to parse the heterogeneity into behaviorally-defined subtypes began with the work of Wing and Gould (1979), who identified three general phenotypes: "aloof" individuals who rarely made social approaches or responses, "active but odd" individuals who often engaged in social interactions but had poor quality of social approaches and responses, and "passive" individuals who responded to others' initiations but rarely engaged in spontaneous social approach. Over time, autism subtype classification went through a number of modifications, and by the mid-1990's, the official diagnostic nomenclature for subtypes of ASD included Autistic Disorder,

Asperger's Disorder, and Pervasive Developmental Disorder, Not Otherwise Specified (King, Navot, Bernier, & Webb, 2014; Volkmar & McPartland, 2014). Despite efforts to refine diagnostic subtypes, these heuristic behavioral categorizations were insufficiently distinct and continually failed to provide insight into differential treatment response (King et al., 2014). Given these shortcomings, the field moved to collapse all behavioral subtypes into a single diagnostic label of autism spectrum disorder in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5; American Psychiatric Association, 2013). Investigations are now underway to discover novel ways to meaningfully subtype this heterogenous population.

Parsing the Heterogeneity

Investigations into child characteristics as moderators of treatment outcomes have been limited. Some intervention efficacy studies have included secondary analyses of baseline measures as potential predictors of differential response to intervention and have revealed intellectual and language ability, adaptive functioning, and chronological age, to be the most consistent moderators (Eapen, Crncec, & Walter, 2016; Howlin et al., 2009; Perry et al., 2011; Reichow et al., 2018; Zachor & Ben-Itzchak, 2017). However, these predictors are limited in that they are atheoretical. They are not intervention-specific and, thus, do not provide utility in individualizing interventions.

Among the first studies to formally investigate child characteristics as moderators of response to treatment was that of Sherer and Schreibman (2005). Scherer and Schreibman (2005) divided participants from archived data into "responder" and "nonresponder" groups based on most and least posttreatment gains, respectively, on standardized assessment and behavioral measures. The researchers developed profiles of the two groups using archived video data from PRT intervention participants with ASD. They discovered a number of characteristics common

to those who benefited most from the intervention (i.e., responders), including moderate to high toy interest, tolerance of others' close proximity, low to moderate non-verbal self-stimulatory behavior, and moderate to high verbal self-stimulatory behavior. Non-responders, on the other hand, had characteristics of low social approach, low toy play, low verbal self-stimulatory behavior, moderate non-verbal self-stimulatory behavior, and moderate avoidance. Six new subjects with ASD (3-5 years old) were then screened into the "responders" ($N = 3$) or "non-responders" ($N = 3$) group based on pre-intervention behavioral coding and matched on age, IQ, symptom severity, and language level. Subjects completed an intensive PRT intervention. Using a multiple baseline design, Sherer and Schreibman (2005) found the behavioral profiles correctly predicted response to treatment. This preliminary study was limited by its small sample size and specificity of behavioral profiles. That is, only a limited number of individuals with ASD would fall under either of the behavioral profiles.

Schreibman, Stahmer, Barlett, and Dufek (2009) performed a follow-up study minimizing the number of child characteristics in a profile. The study included two- to four-year-old children with ASD assigned to one of two behavioral profiles: 1) high toy contact and high avoidance ($N = 3$) and 2) low toy contact and low avoidance ($N = 3$). Toy contact was operationalized as appropriate interactions with toys, and avoidance was operationalized as the child moving away from an adult out of arm's reach. Participants completed PRT followed by DTT intervention. A multiple baseline design was employed with frequency of spontaneous and cued vocalizations as outcome variables. In the high toy contact - high avoidance group, all participants had increased vocalizations. In the low toy contact - low avoidance group, one participant did not improve and two participants had increased vocalizations. The authors noted one of the participants in the low toy contact - low avoidance group "switched" profiles during

the intervention phase, displaying characteristics of high toy contact, after which he showed dramatic improvement. Schreibman and colleagues (2009) concluded toy contact may predict PRT outcomes but not DTT outcomes, and that avoidance did not appear to be a predictor of treatment outcomes. This study design showed strength in comparing two different types of intervention and demonstrated a potential for a particular child characteristic (i.e., appropriate interaction with toys) to be a predictor of a specific type of intervention (i.e., PRT). However, their sample was limited and outcome differences between individuals with different profiles were not robust.

Fossum and colleagues (2018) performed another follow-up study on Sherer and Schreibman's (2005) study with a larger sample size ($N = 57$) of preschoolers with ASD enrolled in a 12-month community-based PRT intervention. They investigated elements of the behavioral profile developed by Sherer and Schreibman (2005) as individual pre-treatment predictors of treatment outcomes. Pretreatment variables included toy contact, avoidance, stereotyped/repetitive vocalizations, and positive affect, along with chronological age, ASD severity, cognitive ability, and baseline expressive language level. Cognitive ability, positive affect, and levels of toy contact each predicted post-intervention expressive language level, together accounting for 40% of variance. This study demonstrated strengths in highlighting contributions of individual characteristics to variable treatment outcomes.

Klintwall and Eikeseth (2012) investigated social and automatic reinforcers as predictors of learning rate in an early intensive behavioral intervention. Learning rate was operationalized as change in age equivalence in the Vineland Adaptive Behavior Scales from pretest to posttest. Reinforcers were determined using the Socially Mediated and Automatic Reinforcer Questionnaire (SMARQ; Klintwall & Eikeseth, 2012). Klintwall and Eikeseth (2012) found

number of social reinforcers was positively correlated with learning rate, whereas number of automatic reinforcers was negatively correlated with learning rate.

Klintwall and colleagues (2015) further investigated interest level as a predictor of later outcomes in 70 toddlers with ASD. They developed a novel video-coding procedure capturing interest level in objects and activities during the ADOS-T. Items were scored on a 5-point Likert scale and averaged across all 10 items for a total interest level score. They found interest level predicted growth in adaptive functioning, along with verbal and nonverbal mental age, over the course of one year.

Thus far, investigations into child characteristics in response to intervention have lacked either theoretical foundation or utilize measures that present a challenge to broad access. Those lacking theoretical foundation seek to parse heterogeneity via broad measures such as IQ or adaptive functioning tests. These variables are unlikely to provide utility in individualizing interventions but may rather predict how an individual will respond to intervention in general. More recent studies have primarily investigated some form of object interest as a variable characteristic of individuals with ASD. This points to a potential variability in underlying reward processing functioning and is theoretically tied to variability in reinforcement-based learning in early interventions. However, many of these studies use video-coding methods to quantitatively measure object interest. This long and arduous process is difficult to replicate at scale, given scarce resources. Currently, investigations are pursuing more efficient, novel ways to parse the heterogeneity, including utility of biomarkers such as eye-tracking. However, these investigations have primarily focused on the diagnostic or screening utility of these biomarkers. Can these biomarkers be utilized as predictors of response to intervention? Some things should be true in order to be an effective predictor. First, the measure should be linked to theoretical

foundations of ASD and treatment. Second, the measure should show adequate construct validity; that is, it should measure what it says it measures. Finally, the resolution of data should adequately reflect individual variability. The next chapter focuses on a predominant theory of ASD, the social motivation hypothesis, as a starting point to discover potential theoretically-based predictors.

CHAPTER 2: LITERATURE REVIEW

Limited understanding of how to individualize interventions and scarce resources have presented a state of poor access to optimal outcomes for many individuals with ASD. Thus far, it is clear that current interventions for ASD draw on varying levels of reinforcement-based learning and focus on varying stages of social communication development. In addition, recent investigations of child characteristics have revealed a common thread of object interest as a potential predictor of intervention effectiveness. These ideas suggest motivation as a differentiating characteristic among individuals with ASD. The social motivation hypothesis, a predominant theory of ASD, may provide a theoretical foundation upon which to discover potential efficient and effective predictors for response to intervention.

Social Motivation Hypothesis

The social motivation hypothesis proposes that core deficits associated with ASD stem from a primary deficit in processing the reward value of social stimuli, resulting in lower basic visual attention to social information (e.g., faces, gaze direction; Dawson et al., 2004). This, in turn, reduces social learning opportunities, including engagement in joint attention, collaborative play, and friendship, ultimately resulting in poor social skill development. The social motivation theory highlights a network of brain regions involved in social reward processing, including the amygdala, ventral striatum, and orbital and ventromedial regions of the prefrontal cortex, forming an orbitofrontal-striatum-amygdala network. These brain regions have been extensively studied in individuals with ASD, and differences have been found in structure (Ecker et al., 2010; Estes et al., 2011; Hollander et al., 2005; Langen, Durston, Staal, Palmen, & van Engeland, 2007; Langen et al., 2009; Mosconi, Cody-Hazlett, et al., 2009; Munson et al., 2006; Nickl-Jockschat et al., 2012; Ohta et al., 2016; Rojas et al., 2006; Schumann et al., 2004; Sears et

al., 1999), function (Delmonte et al., 2012; Di Martino et al., 2011; Kohls et al., 2013; Shafritz, Dichter, Baranek, & Belger, 2008; Turner, Frost, Linsenbardt, McIlroy, & Müller, 2006), and regional gene expression (Bear, Huber, & Warren, 2004; Peça et al., 2011; Reiss, Abrams, Greenlaw, Freund, & Denckla, 1995).

Studies investigating social reward processing have found some support for the social motivation hypothesis (Bottini, 2018). However, when studies included both social and non-social stimuli, aberrations in reward processing in the ASD sample compared to typically developing controls were generally observed in both stimuli types (Bottini, 2018; Dichter, 2018). That is, evidence is accumulating in support of broader motivational impairments, rather than those specific to social stimuli. For example, Clements and colleagues (2018) completed a systematic review and meta-analysis of functional MRI studies investigating reward processing in individuals with ASD. They found that for both social and nonsocial rewards, individuals with ASD showed aberrations in activation of reward-processing regions, including hypoactivation in bilateral caudate and anterior cingulate cortex and hyperactivation in the putamen and insula. They also found increased widespread reward circuitry activation in response to restricted interests.

In addition to general reward-processing deficits, striking heterogeneity within ASD samples is continually cited (Bottini, 2018), and the social motivation hypothesis likely explains only a subset of individuals with autism spectrum disorder. Deficits posited in the social motivation hypothesis may provide utility in explaining the variable effectiveness of interventions based heavily on reinforcement learning principles. Investigating basic behavioral processes may provide clues to underlying reward processing impairments.

Social Motivation Hypothesis and Basic Behavioral Processes

From the perspective of the social motivation hypothesis, intact reward processing is necessary for intact basic behavioral processes, including social orienting, response to joint attention, and initiation of joint attention. Social orienting is an individual's "ability to spontaneously orient to naturally occurring social stimuli in their environment (Dawson et al., 2004, p. 272)." Involuntary, or reflexive, social orienting appears within the first weeks of life in typical development. Volitional social orienting, such as orienting when one's name is called, typically emerges within five to seven months of age. Attention to specific stimuli has been shown to be facilitated by reward processing neurocircuitry. Neuroimaging studies have identified reward-related neural regions, including the anterior cingulate cortex (ACC) and striatum, in modulating visual attention (e.g., Pessoa & Engelmann, 2010), and electrophysiological studies have shown that ERP measures of attention are closely linked to reward anticipation (Kohls et al., 2011). Response to reward feedback in the anterior cingulate cortex has also been shown to predict the magnitude of reward-driven visual attention (Hickey, Chelazzi, & Theeuwes, 2010). Aberrations in visual social attention may be indicative of underlying reward processing deficits.

Social orienting has been shown to be abnormal in individuals with ASD (Dawson, Bernier, & Ring, 2012; Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998; Dawson et al., 2004; P. Mundy & R. Neal, 2001; Peter Mundy & R. Neal, 2001; Mundy, Sigman, Ungerer, & Sherman, 1986; Shultz, Klin, & Jones, 2018). For example, using a naturalistic experimental paradigm to investigate social attention in young children with ASD, Dawson and colleagues (1998; 2004) found the ASD group oriented to social stimuli significantly less than developmentally delayed and typically developing peers. Interestingly, impairment was also

observed in orienting toward non-social stimuli, paralleling findings in the reward processing literature.

Joint attention behavior (JA) involves two components: response to joint attention (RJA), which involves following another's eye gaze to a target object, and initiation of joint attention (IJA), which involves seeking another's attention using eye gaze with the purpose of drawing the other's attention to a shared experience. Development of joint attention typically occurs within six to nine months of age. Neuroimaging evidence supports the involvement of reward-related neurocircuitry in IJA and RJA behavior (Mundy, 2018). For instance, Oberwelland and colleagues (2016) found that IJA and RJA tasks activated reward-related neural regions, including the ventral striatum, medial frontal cortex, and amygdala in school-aged children. Similar results were found with infant and toddler cohorts (Eggebrecht et al., 2017). Another study found a direct relationship between increased frontolimbic neural circuit connectivity at six months and subsequent RJA abilities at nine months in TD individuals (Elison et al., 2013). Billeci and colleagues (2017) found delta band increase in IJA task; delta band has been linked to learning, motivation and reward processes. Reduced responses to joint attention and bids for joint attention in individuals with ASD have been widely reported on behavioral tasks (Gredebäck, Fikke, & Melinder, 2010; Leekam & Ramsden, 2006; Mundy, Sullivan, & Mastergeorge, 2009).

Social Attention Eye-Tracking Measures

Eye-tracking measures of social attention have burgeoned over the last decade and properties of these types of measures may provide particular utility in broad and accessible precision treatment. First, they are efficient- eye-tracking paradigms that can be completed within a few minutes. Second, they capture a higher resolution of data relative to traditional

behavioral data (i.e., data based on human observation), increasing the probability of detecting variability among individuals. Third, minimal training is required to administer an eye-tracking measure and can thus be feasibly administered by lay providers. Thus far, these measures have largely been used to identify differences between individuals with ASD and without ASD. However, given that great variability exists within the ASD population in terms of social motivation and downstream behaviors, such as social orienting, eye-tracking measures of social attention provide a promising avenue to advance precision treatment by capturing this variability and relating this dimension to intervention outcomes.

Basic visual social attention. Numerous eye-tracking measures have been developed in recent years to represent several aspects of social attention. A majority of these represent basic attention toward social stimuli, including social games, biological motion, activity monitoring, "Sandwich Lady," static images, goal-related orienting, and social-geometric preferential looking (see Table 1). Results generally show lower looking time toward social stimuli for ASD groups than typically developing or developmentally delayed groups.

Table 1.
Eye-Tracking Measures of Basic Visual Social Attention

Measures	Description	Results
Social Games (Jones, Carr, & Klin, 2008; Jones & Klin, 2013)	10 video clips of an actress looking directly into the camera performing social games (i.e., peek-a-boo)	- Toddlers with ASD looked less at the actress's eyes and more at the mouth than developmental delayed and typically developing toddlers, - Percentage of fixation on eyes negatively correlated with ASD severity - Decreased looking toward faces in infants with ASD who were 6 months to 2 years old.
Biological Motion (Falck-Ytter, Rehnberg, & Bölte, 2013; Klin, Lin, Gorrindo, Ramsay, & Jones, 2009)	Point-light animations of children's games in a preferential looking task with one side of the screen showed upright animations while the other showed inverted animations	- Toddlers with ASD spent significantly less time looking at the upright animations relative to the inverted animations than control groups. The ASD group spent about the same time on both types of animations. - When physical contingency was included (audio visual synchrony), such as the sound of a clap when point lights collide, no difference was found among groups. - Similar differences found in 3-4 year old children with ASD.
Activity Monitoring (Shic, Bradshaw, Klin, Scassellati, & Chawarska, 2011)	Video scenes of two individuals engaging in a simple activity together	-Toddlers with ASD looked less at the activity in a video scene and more at the background objects than typically developing toddlers and those with developmental delays.
Sandwich Lady (Chawarska, Macari, & Shic, 2012)	3-minute dynamic video scene featuring an actress at the center of the screen addressing the participants directly while engaging in a sandwich making activity or drawing attention to one of four objects located in each corner of the screen	- Decreased looking at the face of an actress looking directly at the camera and providing dyadic cues for attention, and decreased looking at the entire screen in toddlers with ASD relative to typically developing and developmentally delayed control groups. Differences were not found when the actress was looking down with no dyadic cues. Decreased attention to social scene, but not objects, and decreased percentage of looking at person in six-month-old infants later diagnosed with ASD.
Static Images (Elsabbagh, Fernandes, et al., 2013; Elsabbagh, Gliga, et al., 2013)	Social versus object stimuli in a static array presentation	- No difference between infants later diagnosed with ASD and control groups in attention to social versus object stimuli in a static array presentation.

Static Images (Amso, Haas, Tenenbaum, Markant, & Sheinkopf, 2014)	16 static images of indoor and outdoor scenes with a single person in them	- Preschool children with ASD spent more time looking at primary, or most salient, AOI, regardless of social or nonsocial quality than typically developing peers. - Increased reliance on salience of AOI was found to be correlated with increased ASD severity scores on the ADOS.
Static Images (Sasson & Touchstone, 2014)	Static social versus nonsocial preferential looking task; Social stimuli include faces with different emotions and object stimuli were either common circumscribed interests and non-circumscribed interests	- Decreased percentage of fixation time on face, increased latency to first fixation on face, and decreased fixation time per visit to face in preschool children with ASD compared to typically developing peers, but only in the circumscribed interest condition.
Goal-Directed Orienting (Vivanti, Trembath, & Dissanayake, 2014)	Videos of an actor moving both arms toward objects in different directions, with or without looking at the target object	- Percentage of visual attention to target and actor's face were greater in head-turning condition compared to the neutral condition in typically developing preschool children (not ASD group) and percentage of attention to the actor's action was greater in the neutral condition compared to the head turning condition only in typically.
Social-Geometric Preference (Franchini et al., 2017; Moore et al., 2018; Pierce, Conant, Hazin, Stoner, & Desmond, 2011; Pierce et al., 2016)	Preferential looking paradigm with dynamic social images (DSI) displayed on one half of the screen and dynamic geometric images (DGI) displayed on the other half	- Toddlers with ASD looked less at the social scene than toddlers without ASD. - Results replicated with preschool children and with varying complexity of social stimuli.

Of the basic visual attention paradigms developed, Pierce's (2011) social-geometric preferential looking eye-tracking task (SocGeoPref-ET) may be well-suited as a potential predictor. The SocGeoPref-ET is a preferential looking paradigm with dynamic social images (DSI) displayed on one half of the screen and dynamic geometric images (DGI) displayed on the other half. Toddlers with ASD looked less at the social scene than toddlers without ASD. In particular, 40% of toddlers with ASD spent over 50% of the time looking at geometric images and half of those toddlers spent over 70% of the time looking at geometric images. In contrast, only 1.9% of typically developing peers and 9% of developmentally delayed toddlers viewed geometric images over 50% of the time and none spent more than 70% of the time looking at geometric images. This finding was robust through IQ-matched comparison, and no age or ADOS severity effects were found. Over the course of the 1-minute video, there was a small but significant increase in percentage of time looking at geometric images in all groups. Number of saccades was greater in ASD than other groups when viewing social images and less in ASD than the typically developing group when viewing geometric images. Test-retest reliability revealed the eye-tracking measure was relatively stable with mean change in looking duration percentage at 15.6% between time 1 and time 2 (between 1 and 14 months).

Pierce and colleagues (2016) performed follow-up study using the same video stimuli with a larger sample and more control groups. With a >69% DGI fixation duration cut-off, sensitivity for ASD diagnosis was 21% while specificity was 98%. Pierce and colleagues (2016) identified a robust subset of toddlers with ASD who highly preferred DGI. When comparing toddlers with ASD who were geometric responders (i.e., >69% DGI) to those with ASD who were social responders (i.e., >69% DSI), geometric responders showed more difficulties in cognitive, language, and social communication than social responders. There was an effect of

age, and the authors extrapolated that the eye-tracking measure detect attentional differences in children older than four years old.

Franchini and colleagues (2017) adapted the SocGeoPref-ET paradigm (2011; 2016) with preschool children with ASD and typically developing controls. They were able to independently replicate Pierce's (2011; 2016) findings using different but conceptually similar stimuli in an older age range (i.e., preschool children rather than toddlers). In analyzing relationships with clinical characteristics, they found increased percentage of looking time on DSI was positively associated with average fixation duration, ESCS joint attention, and VABS socialization and communication scales, and negatively associated with number of saccades on DSI. Finally, ESCS joint attention was positively correlated with VABS communication scale. Gender distribution was not equal but post-hoc analyses revealed no significant differences between males and females on various measures.

Pierce's group (Moore et al., 2018) tested two different versions of dynamic social images. The Original SocGeoPref-ET paradigm, which utilizes Pierce and colleagues' (2011) original stimuli with one individual per video clip, and the Complex SocGeoPref-ET paradigm, which replaces single individuals with two children interacting. No difference was found in the robustness of findings regarding complexity of social stimuli. Geometric responders had significantly greater ADOS severity scores, lower Mullen receptive language scores, and lower VABS motor domain scores than social responders.

Notably, Pierce's group (Moore et al., 2018; Pierce et al., 2011; Pierce et al., 2016) found striking heterogeneity in visual social attention within ASD groups. Many ASD individuals performed similarly to control groups, while a subtype of ASD emerged with individuals with the most extreme atypical visual social attention (namely, geometric responders). These

responders showed greater autism symptom severity. Franchini and colleagues (2017) also found this ASD-specific heterogeneity.

The SocGeoPref-ET paradigm (Pierce et al., 2011) has potential as a predictor because its effects are robust across minor changes in stimuli and have been replicated independently. Other paradigms have not shown differences between groups or their ecological parallels are more difficult to determine. Importantly, the authors have clearly shown immense variability in results among individuals with ASD. If differences in social attention among individuals with ASD do predict intervention effectiveness, this measure has adequate variability to detect correlations. However, construct validity has not been demonstrated, so it is unclear whether the SocGeoPref-ET paradigm truly measures basic visual social attention.

Response to joint attention. Eye tracking measures of joint attention have been investigated less often than measures of visual social attention. Those that have studied joint attention have mainly focused on *response* to joint attention and yielded mixed results. Several 'response to joint attention' paradigms and one 'initiation of joint attention' paradigm have been developed to date. Bedford and colleagues (2012) investigated gaze following and attentional engagement in a response to joint attention eye-tracking task. Fifty-four infants at-risk for ASD (i.e., infants with older siblings diagnosed with ASD) and 50 low-risk controls were seen at seven months and again at 13 months. At-risk infants were sub-grouped into atypically developing sibling (AT-sibs), autism spectrum disorder siblings (ASD-sibs), and typically developing siblings (TD-sibs) depending on their clinical presentation at 36 months. No group differences were found in accuracy of gaze shifts at either time point, but atypically developing siblings and ASD siblings had significantly reduced looking time toward the attended object than

control groups. Looking time toward attended object at 13 months was negatively correlated with ASD severity scores at 24 months only for the AT-sibs group.

Navab and colleagues (2012) also investigated an eye-tracking measure of response to joint attention in infants at-risk for ASD. They found that standard difference score and percentage of accurate gaze shifts were positively correlated with the Early Social Communication Scales distal response to joint attention score. However, percentage of accurate gaze shifts was lower for the eye-tracking task than for the ESCS. Eye-tracking measures of RJA were not correlated with language measures or ASD severity.

Falck-Ytter and colleagues (2012) investigated a RJA eye-tracking measure in preschool children with ASD compared to developmentally delayed and typically developing controls. Participants with ASD had significantly lower gaze shift accuracy (i.e., difference scores) and slower gaze shifts than typically developing participants. Follow-up analyses revealed verbal IQ was the driver of the latter correlation. For the ASD group, VABS-II communication score predicted RJA accuracy. Nonverbal IQ was correlated with total number of gaze shifts, but not accuracy of gaze shifts.

Falck-Ytter and colleagues (2015) also investigated RJA eye-tracking in younger preschool children (2-5 years old) with ASD, developmental delays, and typically developing controls. They found no differences among groups in RJA accuracy. However, first fixation duration to attended versus unattended object was also measured. ASD individuals had significantly lower difference scores than typically developing toddlers and developmentally delayed chronologically age-matched controls. ASD group and typically developing chronologically age-matched controls showed no significant between group differences, although there was a trend with moderate effect size.

Billeci and colleagues (2016) studied RJA eye-tracking task in toddlers with ASD and typically developing controls. They found no significant differences in eye-tracking measures of RJA between groups. However, number of transitions from face to object correlated negatively with ADOS item A7 (pointing). Lower number of gaze transitions predicted more difficulty with pointing.

Response to joint attention eye-tracking stimuli are largely consistent across experiments. Generally, an actor is shown at the center of the screen with objects placed at either side of the actor. The actor draws attention toward one of the two objects using eye gaze and/or pointing. Although evidence is mixed regarding mean differences between ASD and typically developing groups, several correlations with behavioral measures have been found, including ASD severity, adaptive communication, nonverbal IQ, and pointing. In addition, preliminary evidence exists for construct validity of this paradigm (Navab et al., 2012). Further examination of the properties of this paradigm as well as replication of construct validity results in preschool children will increase confidence in the use of this measure as a predictor of response to intervention.

Initiation of joint attention. Recently, Billeci and colleagues (2016) developed the first eye-tracking measure to test initiation of joint attention (IJA) in toddlers with ASD and typically developing controls. Toddlers with ASD had significantly more transitions from face to object and object to face than typically developing toddlers. Number of transitions was positively correlated with ADOS item B1 (eye contact). In other words, a higher number of transitions between face and object predicts more difficulty with eye contact on the ADOS. Billeci and colleagues (2016) also found greater fixation duration to the face in the ASD group relative to the typically developing group. Construct validity has not been established and results appear

counterintuitive. As the only initiation of joint attention paradigm developed, it is worth further investigating the properties and construct validity of the paradigm.

Social Attention Eye-Tracking Measures as Predictors of Response to Intervention

Can these paradigms be used to predict response to intervention? To date, only one study has investigated eye-tracking measures of social attention as predictors of response to intervention. Vivanti and colleagues (2013) studied predictors of treatment outcomes in preschool children receiving a one-year group ESDM intervention. ESDM was developed based on the concept that early learning occurs through socially rewarding activities. Vivanti and colleagues (2013) hypothesized that individuals with higher ability to participate in social learning activities, then, would benefit more from treatment. They investigated skills foundational to early social learning, including functional use of objects, understanding goals behind others' actions, social attention, and imitation. They found that functional object use, goal understanding, and imitation predicted various aspects of change in cognitive functioning but not ASD severity. Social attention, measured using an eye-tracking paradigm, did not predict change in cognitive functioning or ASD severity. However, variance data was not included in the published results and the authors considered a lack of robustness of the particular paradigm to detect differences in social attention. The video stimuli for the paradigm involved an actor and four objects on the screen. Amount of time looking at the actor's face relative to looking at the objects was recorded. Notably, chronological age, pretreatment cognitive functioning, and treatment intensity (although minimum 15 hours) did not predict treatment outcomes.

Along with potential lack of variability, the paradigm used in Vivanti et al.'s (2013) study may lack of construct validity. In order to be a good candidate as a predictor of response to intervention, an eye-tracking paradigm should not only show ability to capture variability within

the ASD population but also adequate construct validity. Since paradigms have been developed to differentiate between ASD and non-ASD populations, there is a paucity of studies investigating the construct validity of these measures. To date, only one study (Navab et al., 2012) has specifically investigated correlations between behavioral parallel of eye-tracking paradigms. Other studies have investigated clinical correlates of eye-tracking measures of social attention. The majority of these studies correlate eye-tracking performance with ASD severity.

Summary and Statement of Problem

Although early intensive behavioral and developmental interventions have been established as the standard of care regarding interventions for increasing functional skills and decreasing challenging behavior in individuals with autism spectrum disorder (ASD), not all individuals appear to benefit equally from any given intervention (Howlin et al., 2009). Thus far, studies that have investigated child characteristics have found moderators for early interventions, such as "toy interest" for PRT (Sherer & Schreibman, 2005) and "functional object use" for ESDM (Vivanti et al., 2013). However, basic behavioral indicators linking neurodevelopmental mechanisms with intervention responsiveness have not been well explored.

The social motivation hypothesis of ASD posits social communication deficits arise from a foundational deficit in social motivation or attention to social stimuli, which prevents normal development of experience-expectant brain systems, such as face and action perception systems (Dawson, Webb, & McPartland, 2005). The theory highlights a network of brain regions involved in social reward processing, including the amygdala, ventral striatum, and orbital and ventromedial regions of the prefrontal cortex, forming an orbitofrontal-striatum-amygdala network, a network that has been shown to be abnormal in ASD. Recent evidence is accumulating in support of not only social reward deficits, but also broader reward processing

deficits (Bottini, 2018; Clements et al., 2018; Dichter, 2018). However, heterogeneity in the etiology and pathophysiology of ASD has been widely reported, including level of dysfunction in the reward learning circuitry. Deficits posited in the social motivation hypothesis may provide utility in explaining the variable effectiveness of interventions based heavily on reinforcement learning principles. From a neurodevelopmental framework, aberrations in the development of neural circuitry for reward processing would result in observable basic behavioral and physiological indicators, which may serve as predictors of response to reinforcement learning-based interventions. Such indicators may include visual social attention and joint attention, evidenced to involve the corticostriatal pathway.

A large number of studies have investigated visual social attention in individuals with ASD using eye-tracking methods. Jones and Klin (2013) found decreased looking toward faces in infants with ASD who were 6 months to 2 years old. Many studies support these findings (Chawarska, Macari, & Shic, 2013; Elsabbagh et al., 2014). In previous studies by Pierce and colleagues (2011; 2016) a subset of toddlers with ASD were found to prefer dynamic geometric images relative to dynamic social images. These toddlers were found to have more severe cognitive, adaptive, and social deficits. Franchini and colleagues (2017) extended this finding to preschoolers with ASD. They observed reduced orienting to dynamic social stimuli and reduced first fixations to dynamic social stimuli in the ASD group relative to typically developing preschoolers. They also found great heterogeneity within the ASD sample.

Reduced responses to joint attention and bids for joint attention have also been widely reported on behavioral tasks (Gredebäck et al., 2010; Leekam & Ramsden, 2006; Mundy et al., 2009) and have begun to be investigated via eye-tracking studies (Billeci et al., 2016; Billeci et al., 2017; Chawarska, Klin, & Volkmar, 2003; Falck-Ytter et al., 2012; Falck-Ytter et al., 2015).

Studies have mainly focused on RJA and gaze accuracy (Chawarska et al., 2003; Falck-Ytter et al., 2012; Falck-Ytter et al., 2015) and have found variable results, with some studies finding fewer and slower gaze shifts in ASD versus typically developing individuals, while others finding no differences in RJA. Billeci and colleagues (2016) recently included an IJA eye-tracking condition and found that differences between ASD and typically developing individuals emerged for IJA, but not RJA, tasks.

The use of eye-tracking methods to measure these behaviors may be particularly valuable, as they are efficient and accessible to individuals of varying ages and skills levels. Thus far, studies have shown some evidence of differences between ASD and typically developing control groups on eye-tracking measures of these behaviors, and, importantly, have found substantial heterogeneity within the ASD group. Less well known are how well these eye-tracking measures associated with behaviors in a real-world setting and whether they may serve as predictors of reward learning skill. Studies have shown decreased basic visual social attention correlates with increased autism symptom severity but have not investigated correlations with behavioral measures of social attention specifically (Moore et al., 2018). Preliminary evidence supports the construct validity of eye-tracking measure of RJA in one study with 18-month old infants (Navab et al., 2012). An eye-tracking measure of IJA has recently been developed (Billeci et al., 2016) and construct validity has not been established. Billeci and colleagues (2016) found frequency of gaze transitions between face and object was positively correlated with ADOS item B1, in which higher scores indicate more unusual eye contact. However, the ADOS item does not delineate the nature of unusual eye contact, and frequency of IJA on the ADOS was not analyzed. This study will investigate the properties and relationships of these

eye-tracking measures of social attention with more ecological, behavioral assessments of social attention.

Specific Aims and Hypotheses

Aim 1 is to examine social attention in young children with ASD as well as early social communicative abilities such as response to joint attention (RJA), and initiation of joint attention (IJA). To achieve this aim, I will compare young children aged 2-6 with ASD ($N = 20$) to typically developing peers (matched on chronological age and gender) on eye-tracking measures using previously developed paradigms: Pierce's (2011) SocGeoPref (basic visual social attention), Billeci's (2016) response to joint attention, and Billeci's (2016) initiation of joint attention. We anticipate group differences in basic visual social attention, RJA, and IJA.

Aim 2 is to relate behavioral indicators of social attention to eye-tracking measures of social attention across: a) basic visual social attention; b) response to joint attention; and c) initiation of joint attention. Using correlational analysis, I will examine the relationship between social attention constructs derived through eye-tracking and corresponding constructs measured using the *SOC-RS*. I hypothesize that eye-tracking measures of basic visual social attention and response to joint attention will correlate positively with corresponding behavioral measures of social attention, whereas the initiation of joint attention eye-tracking measure will negatively correlate with the behavioral measure of initiation of joint attention.

The first step in evaluating these eye-tracking measures of social attention as potential predictors of response to intervention is understanding the properties (aim 1) and the construct validity (aim 2) of the eye-tracking measures. This will provide foundational knowledge to understand the utility of these measures as predictors of response to intervention. Therefore, with the above aims, I seek to address the following research questions:

1) What are the properties of eye-tracking measures of social attention, including range and variability, in children with ASD, compared to typically developing children?
2) Do eye-tracking measures of social attention show construct validity when compared with more ecological behavioral measures, controlling for age, nonverbal IQ, and diagnosis?

CHAPTER 3: METHODOLOGY

Participants

Participants were 20 preschool children from 2-6 years old with ASD along with 22 chronological age and gender-matched typically developing (TYP) children. Participants were recruited from a local autism center, a local university recruitment pool, and flyers at local daycare and community centers. All ASD subjects met criteria for an ASD diagnosis based on the "gold standard" assessment using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2; Lord et al., 2012), Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994), Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003), and clinical judgement with use of DSM-5 criteria (American Psychiatric Association, 2013). Typical controls do not have a diagnosis of ASD, other developmental delay, or presence of a learning or language disability. All subjects have normal or corrected to normal vision.

Measures

Several eye-tracking and behavioral observational outcome variables were used for this study. Eye tracking variables included visual social attention, response to joint attention, and initiation of joint attention. Behavioral observational variables included social referencing, response to joint attention, and initiation of joint attention. In addition to outcome measures, several measures were administered to characterize the participant sample, including the ADOS-2 (Lord et al., 2012), ADI-R (Lord et al., 1994), SCQ (Rutter et al., 2003), Mullen Scales of Early Learning (MSEL; Mullen, 1995) and Vineland Adaptive Behavior Scales, Third Edition (VABS-3; Sparrow, Cicchetti, & Saulnier, 2016). Measure descriptions are as follows:

Visual social attention (SocGeoPref-ET). Visual social attention was assessed using percentage of time spent looking at the social target in an eye-tracking preferential looking task with dynamic geometric scenes and dynamic social scenes. We designed the social-geometric preferential looking eye-tracking task (SocGeoPref-ET) based on a task developed by Pierce and colleagues (2011). Following a central fixation (1.5 s), children were presented with two movies, one dynamic social image and one dynamic geometric image (16 s). There was a total of 3 Blocks (6 trials) with target side counterbalanced.

Response to joint attention-eye-tracking (RJA-ET). RJA-ET was measured using percentage of valid trials with accurate first gaze shifts from face to object in an eye-tracking response to joint attention task. We designed the response to joint attention task based on a task developed by Billeci et al. (2017). Following a central fixation (1.5 s), children were presented with a video consisting of a neutral background and a model wearing a neutral-colored shirt and hair tied back. Two colorful, identical toy structures were placed in front and on either side of the model, atop a neutral colored table. During the baseline period, the model's gaze remained fixed on the table in front of her (~2 seconds). This phase was followed by a social greeting phase (~2 seconds), during which the model looked into the camera, smile, and say "Hello there." In the final stage, for the first condition, the model stated "look" as she turned her head toward one of the two objects and then fixated on the object (~4 seconds); for second condition, the model stated "look" and pointed to the object as she turned her head toward one of the two objects and then fixated on the object (~4 seconds). Each condition had 3 trials (2 blocks, 6 total trials) with target object side counterbalanced.

Initiation of joint attention-eye-tracking (IJA-ET). IJA-ET was measured using number of gaze transitions per trial between face and target object in an eye-tracking initiation of

joint attention task. An IJA eye-tracking paradigm has recently been developed, and differences among young children with ASD and TYP have been noted (Billeci et al., 2016). We designed the initiation of joint attention task based on the task developed by Billeci et al. (2016). Following a central fixation (1.5 s), children were presented with a video consisting of a neutral background and a model wearing a neutral-colored shirt and hair tied back sitting behind a neutral colored table. During the baseline period, the model's gaze remained fixed on the table in front of her (~2 seconds). This phase was followed by a social greeting phase (~2 seconds), during which the model looked into the camera, smile, and said "Hello there." In the final stage, the model kept gaze directed toward camera with neutral, impassive facial expression as a toy appeared unexpectedly from outside the scene and crosses toward opposite side of screen (~7 seconds). 3 trials were administered with target object side counterbalanced.

Social Orienting Continuum and Response Scale (SOC-RS). The SOC-RS (Mosconi, Reznick, Mesibov, & Piven, 2009) is a dimensional measure of social orienting behavior in preschool children coded based on videos of ADOS-2 administrations. Interrater reliability, calculated using intra-class correlation coefficients, was .91 for social referencing. Internal consistency was adequate, ranging from .78 and .72. Correlations between the SOC-RS and VABS-Socialization subscale and between SOC-RS and VABS-Motor subscale were examined to assess convergent validity. SOC-RS item scores and VABS-Socialization subscale scores were significantly associated, while only orienting to name on SOC-RS was significantly associated with VABS-Motor scores.

Training and reliability. Two graduate student raters, including the author of the study, were trained on the SOC-RS using guidelines provided in the measure's manual (Mosconi, Reznick, et al., 2009). Videotaped ADOS-2 sessions were coded using procedures specified in

Mosconi et al. (2009). The raters were blind to eye-tracking results during coding. To establish reliability on the SOC-RS, the author of the study and second rater independently coded ADOS-2 videos, and reliability was calculated separately for each SOC-RS item. Raters then met and discussed ratings until consensus was reached. Once interrater reliability was over 80% agreement across three consecutive complete videos, the remaining videos were independently coded by reliable raters. In order to minimize observer drift, both the author and reliable second rater independently coded 20% of the ADOS-2 videotapes at three time points spread over the course of the study in order to ensure continued reliability.

Social referencing. To assess the behavioral analogue of the SocGeoPref-ET visual social attention measure, social referencing was assessed using an adaptation of the SOC-RS social referencing measure. Social referencing on the SOC-RS is defined as an event in which the participant child fixates his or her gaze on another individual's face. The original variable was based on number of fixations greater than 2 seconds upon another's face per minute of observable time. In order to increase interrater reliability, our adapted variable was calculated based on total gaze duration upon another's face per minute of observable time. As such, video coding of social referencing was accomplished as a state event (i.e., recording "start" and "stop" times of the behavior) rather than a point event (i.e., recording whether an instance of the behavior occurred).

Response to joint attention-behavioral observation (RJA-BO). RJA-BO was assessed using the response to joint attention score in the SOC-RS, which results in a derived score of 0 or 1. As noted above, the SOC-RS is a dimensional measure of social orienting behavior in preschool children coded based on videos of ADOS-2 administrations. The coded ADOS-2 activity consists of an examiner performing bids for joint attention including in a graduated

manner. The examiner will first deliver three attempts by gazing toward the target object and saying, “Look!” or “Look at that!” If the child does not respond to the first attempts, the examiner then additionally points to the target while gazing toward the target and saying, “Look at that!” for two attempts. Responses are scored as ‘responders’ if the child follows the examiner’s shift in gaze during the JA task of the ADOS-2 and are scored as ‘non-responders’ if the child does not follow the examiner’s shift in gaze or only follows bids using pointing.

Initiation of joint attention-behavioral observation (IJA-BO). IJA-BO was assessed using the rate of initiations of joint attention per minute of observable time in the SOC-RS. While there is no upper limit to this derived score, based on previous literature using the SOC-RS and reported mean scores on this variable we anticipate a range between 0 and 0.95. Initiation of joint attention is defined as an event in which a participant child evokes another person’s attention, directing it toward an object.

Autism Diagnostic Observation Schedule, Second Edition (ADOS-2). The ADOS-2 is a semi-structured, standardized assessment of an individual’s social interactions, communication, and play skills as well as presence of unusual behaviors (Lord et al., 2012). It consists of five modules, each appropriate for a certain age range and/or speech level. During the assessment standard activities are done to elicit certain behaviors from the examinee relevant to the ASD diagnosis. Behaviors are coded and scored with an algorithm. Items are coded from 0 to 3, depending on severity of abnormality, or 7 for clinically significant abnormalities of the kind not reflect in the item, 8 for not applicable, and 9 for not known. Items are then converted to algorithm scores: “1” and “2” codes remain the same, “3” codes are converted into “2” scores, and all other codes are converted into “0” scores. Two algorithm domains are included: 1) Social Affect and 2) Restricted and Repetitive Behavior (RRB). Cut-off scores for algorithm domains

were assigned to create maximum likelihood that individuals with ASD would score above the cut-offs. Interrater reliability for Modules 1-3 ranged from .92 - .98 for the Social Affect domain, .79 - .91 for the Restricted and Repetitive Behavior domain, and .94 - .97 for the Overall Total score. Test-retest reliability for Modules 1-3 ranged from .81 - . 92 for the Social Affect domain, .68 - .82 for the Restricted and Repetitive Behavior domain, and .83 - .87 for the Overall Total score. In validating individual items, correlation matrices were generated for all items in each module, and items consistently intercorrelated more than .70 were targeted for elimination. Exploratory analyses were performed, in which one major factor emerged in each module. 52% to 53% of variance for Modules 3 and 4 were accounted for by this factor, in which almost all items in Social Interactions and Communication domains loaded. The main factor accounted for 72% to 78% of variance in Module 1 and 2. Regarding item-total correlations, almost all items correlated more with their assigned domain than with each other. Item-total correlation ranges were between .33 and .78 in the Social Affect domain and between .27 and .55 in the Restricted, Repetitive Behaviors domain. Cronbach's alphas were between .87 and .92 for the Social Affect domain and between .51 and .66 for the Restricted, Repetitive Behaviors domain. Also reviewed were item correlations with chronological age and verbal mental age, and findings indicated data was generally not biased by chronological and verbal mental age. Evidence supports strong predictive validity of the ADOS-2 to accurately identify individuals on the autism spectrum. Depending on the module, sensitivity ranged from 91% to 98% and, with one exception, specificity ranged from 84% to 94%. For Module 1, for individuals with few to no words and with a nonverbal mental age of 15 months or less, specificity dropped to 50%. For the Toddler Module, interrater reliability ranged from .74 to .99, test-retest reliability ranged from .60 to .95, sensitivity ranged from 83% to 91%, and specificity ranged from 86% to 94%.

Autism Diagnostic Interview-Revised (ADI-R). The ADI-R is a standardized, structured caregiver interview designed to obtain information in the areas of communication, reciprocal social interactions, and restricted, repetitive behaviors and interests (Lord et al., 1994). The ADI-R includes 93 items. Parent report of behavior is coded and then scored with an algorithm. Items are coded from 0 to 3, depending on severity of abnormality, or 7 for clinically significant abnormalities of the kind not reflect in the item, 8 for not applicable, and 9 for not known. Items are then converted to algorithm scores: "1" and "2" codes remain the same, "3" codes are converted into "2" scores, and all other codes are converted into "0" scores. Four algorithm domains are included: 1) Qualitative Abnormalities in Social Interaction, 2) Qualitative Abnormalities in Communication, 3) Restricted, Repetitive, and Stereotyped Behavior, and 4) manifestation of abnormalities before 36 months. Cut-off scores for algorithm domains were assigned to create maximum likelihood that individuals with ASD would score above the cut-offs. Lord et al. (1994) found good interrater reliability for summated ratings in the three domains, reciprocal social interaction, abnormalities in communication, and stereotyped patterns of behavior, with intraclass correlations between .93 and .97. Chakrabarti and Fombonne (2001) also assessed interrater reliability and found the following intraclass correlation coefficients: .82 for the social section, .87 for nonverbal communication, .85 for verbal communication, .59 for repetitive behaviors, and .86 for the total ADI-R score. Test-retest reliability data was obtained in Lord et al. (1993), and reliability was found to be very high with all coefficients in the .93 to .97 range. Diagnostic validity was assessed by Lord et al. (1994) and ADI-R showed good discriminative validity between individuals with ASD and those with other delays when individuals were 2 years or older.

Social Communication Questionnaire (SCQ). The SCQ is a standardized parent-reported screening measure of autism symptomatology (Rutter et al., 2003). It includes 40 items in yes/no format. Two forms are available: a Lifetime form, which assesses a child's behaviors over his or her entire developmental history, and a Current form, which assesses a child's behaviors within the past three months. One point was designated for each behavior endorsed, and a cut-off score was assigned to create maximum likelihood that individuals with ASD would score above the cut-off. The alpha index of internal consistency was .84 for younger age groups (2-6 years old) and for individuals with no language. Concurrent validity was determined by examining associations with the ADI-R. Pearson intercorrelations across domains ranged from .73 to .92.

Cognitive functioning. Cognitive functioning was assessed using the Mullen Scales of Early Learning (MSEL). The MSEL is an individually administered, norm-referenced standardized assessment of cognitive functioning for infants and preschool children, from birth to 68 months of age (Mullen, 1995). MSEL assesses skills in language, motor, and visual domains and consists of five scales: Gross Motor, Fine Motor, Visual Reception, Receptive Language, and Expressive Language. The Gross Motor scale measures central motor control and mobility. The Visual Reception Scale measures ability to process visual patterns via visual discrimination and visual memory. Skills involved include visual organization, visual sequencing, and visual spatial awareness; and concepts include position, shape, and size. The Visual Reception Scale is thought of as the input side of visual organization skills. The Fine Motor Scale measures visual-motor ability, including unilateral and bilateral manipulation and writing readiness. It involves both visual discrimination (motor planning) and motor control and reflects the expressive side of visual organization. The Receptive Language Scale tests a child's

ability to process linguistic input, including auditory comprehension and auditory memory abilities. These involve the use of auditory organization, sequencing, and spatial concepts. Of note, approximately half the items in the Receptive Language Scale involve both auditory and visual modalities, which requires some degree of auditory-visual integration. The Expressive Language Scale measures productive use of language and includes speaking ability and language formation, including the ability to verbalize concepts. These tasks also require auditory comprehension and auditory memory. Finally, the Early Learning Composite is a measure of general intelligence derived from a composite of Visual Reception, Fine Motor, Receptive Language, and Expressive Language scales. Internal consistency, based on split-half coefficients, was satisfactory for each of the five scales across 17 age groups, with median values ranging from .75 to .83. In addition, the internal reliability of the composite is high, with a median value of .91. Test-retest reliability was .96 for the Gross Motor Scale for the younger age group (1-24 months). For the younger group, stability coefficients ranged from .82 to .85, and for the older age group (25-56 months), stability coefficients ranged from .71 to .79. Interscorer reliability for individual scales for different age groups ranged from .91 to .99. Construct validity was assessed in several ways. Mean raw scores for examinees increase with chronological age, a necessary (but not sufficient) data trend for an assessment of motor and mental abilities for young children who show rapid development in these areas. Concurrent validity was measured with correlations with Bayley Scales of Infant Development, Preschool Language Assessment, and Peabody Fine Motor Scale, which supported both convergent and divergent validity of the Mullen Scales. Independent researchers have found a high degree of specificity, identifying about two-thirds of the children who subsequently experienced failure in kindergarten through second grade. Mullen Scales was also shown to discriminate well between low-birthweight and normal children.

Adaptive functioning. Adaptive functioning will be assessed using the Vineland Adaptive Behavior Scales, Third Edition (VABS-3; Sparrow et al., 2016). The VABS-3 is a standardized parent-reported measure of adaptive functioning in several domains, including Communication, Daily Living Skills, Socialization, and Motor domains, along with an Adaptive Behavior Composite. It is available in both rating form and various interview formats for both parents/caregivers and teachers. For this study, the comprehensive interview format will be used. This format consists of 381 possible core items, which are scored "0" for Never, "1" for Sometimes, and "2" for Usually or Often. Internal consistency coefficient alpha averages range from .90 to .98 for all domains and the composite score. Test-retest reliability averages range from .73 to .92 for domains and from .80 to .92 for the composite score. Interrater reliability correlations range from .70 to .81 for domains and composite. Construct validity was shown through correlations between VABS-3 and other adaptive behavior scales, including the Vineland-II Survey Interview Form, Bayley Scales of Infant and Toddler Development (Bayley-III), and Adaptive Behavior Assessment System, Third Edition (ABAS-3). The Vineland-3 has been validated for use with a variety of clinical samples, including developmental delay, intellectual disability, autism, hearing impaired, and visually impaired groups.

Procedure

Recruitment of individuals with ASD and typically developing individuals occurred through several methods. For both groups, flyers were placed in various daycares and community settings in the local area. Interested families were screened by the researcher over the phone. In addition, for both groups, a research assistant called and/or emailed and screened potential participants from a list of volunteers obtained from a university volunteer participant pool. Recruitment of individuals with ASD also occurred at a local autism center. For families

that have previously consented to being contacted for research opportunities, the researcher approached, recruited, and screened subjects for eligibility. Informed consent was obtained upon check in to the first visit. The researcher reviewed the consent form in its entirety with the family, and the family was given the opportunity to ask questions.

All subjects were assessed individually on a battery of eye-tracking and behavioral tasks over a period of two days to avoid participant fatigue, and parents completed interviews and questionnaires. Direct assessments were recorded and occurred at a local university, the local autism center or the participants' homes. Interviews and questionnaires were conducted in-person at a local autism center, university, participant's home, or over the phone.

One visit occurred at a local university, during which subjects participated in the eye-tracking task. The other visit occurred at a local university or the participants' homes, during which subjects participated in the Mullen and ADOS-2 (~2 hrs, including breaks). The VABS-3 (~1 hr) parent interview occurred in-person at a local autism center, university, participant's home or over the phone. The Social Communication Questionnaire (SCQ) and Child Behavior Checklist (CBCL) parent questionnaire were given to parents to complete. Parents of participants with ASD additionally completed the ADI-R parent interview, which occurred in-person at a local autism center, university, participant's home, or over the phone.

Eye tracking is a non-invasive experiment of measuring an individual's point of gaze on a video screen, as well as pupillary dilation in response to light. The participant sat approximately 60-75 cm from a monitor and an Eye Link 1000 stand-alone eye tracker. Setup involved approximately one minute of adjusting the camera settings to accurately capture the participant's eyes. The participant was asked to watch the screen throughout the session, and was permitted breaks to move around, eat, use the restroom, and so forth as necessary. The stimuli on the

screen varied and included short animations of people and objects. The eye-tracking session, including setup and total testing, lasted approximately 15 minutes. This is believed to be a reasonable burden given the low level of demand on the participant during testing.

At the conclusion of study participation, families were given $50 for their participation and transportation reimbursement, and, upon request, individual results for the developmental assessment were summarized orally.

Analytic Approach

For all analyses, all subjects were individually assigned to group. Therefore, there are no dependence issues regarding sampling or group assignment. Also, since subjects did not undergo treatment in this study, there are also no treatment-based dependence issues.

To achieve Aim 1, I assessed differences between preschoolers with ASD and typically developing peers on eye-tracking measures of attention toward social stimuli and joint attention, controlling for non-verbal IQ and age. For ease of interpretation, metrical predictors were standardized and categorical predictors were effect-coded. Data was analyzed using regression models to probe for group differences in each of the three outcome variables: 1) percent of time spent looking at the social target in a preferential looking task, 2) percentage of trials with accurate gaze shifts in a response to joint attention task, and 3) number of gaze initiations per trial. The model equations are as follows:

$$\text{SocGeoPref-ET} = b_0 + b_1\text{*Dxeff} + b_2\text{*ZNVIQ} + b_3\text{*ZAge} + b_4\text{*Dxeff*ZNVIQ} + b_5\text{*Dxeff*ZAge} + b_6\text{*ZAge*ZNVIQ} + b_7\text{*Dxeff*ZNVIQ*ZAge}$$

$$\text{RJA-ET} = b_0 + b_1\text{*Dxeff} + b_2\text{*ZNVIQ} + b_3\text{*ZAge}$$

+ b_4*Dxeff*ZNVIQ + b_5*Dxeff*ZAge + b_6*ZAge*ZNVIQ + b_7*Dxeff*ZNVIQ*ZAge

IJA-ET = b_0 + b_1*Dxeff

+ b_2*ZNVIQ + b_3*ZAge

+ b_4*Dxeff*ZNVIQ + b_5*Dxeff*ZAge + b_6*ZAge*ZNVIQ + b_7*Dxeff*ZNVIQ*ZAge

To achieve Aim 2, I examined the relationships of eye-tracking measures of visual social attention and joint attention with behavioral assessments of social referencing and joint attention in individuals with ASD. Analyses were completed to test construct validity using a set of regression models. For ease of interpretation, metrical predictors were standardized and categorical predictors will be effect-coded. Analyses controlled for age, nonverbal IQ, and diagnostic status.

Analysis #1 final model was as follows.

SocRef-BO = b_0 + b_1*ZAge + b_2*ZNVIQ + b_3*Dxeff

+ b_4*ZSocGeoPref-ET

+ b_5*ZAge*ZSocGeoPref-ET + b_6*ZNVIQ*ZSocGeoPref-ET + b_7*Dxeff*ZSocGeoPref-ET

In the model above, SocRef-BO, social referencing (standardized number of fixations per minute of observable time), is equal to the conditional mean (b_0), plus the unique effects of age (b_1), nonverbal IQ (b_2), diagnostic status (b_3), SocGeoPref-ET (b_4), age*SocGeoPref-ET interaction (b_5), nonverbal IQ*SocGeoPref-ET interaction (b_6), and diagnostic status*SocGeoPref-ET interaction (b_7).

Analysis #2 final model was as follows.

Logit (RJA-BO) = b_0 + b_1*ZAge + b_2*ZNVIQ + b_3*Dxeff

+ b_4*ZRJA-ET

+ b_5*ZAge*ZRJA-ET + b_6*ZNVIQ* ZRJA-ET + b_7*Dxeff*ZRJA-ET

In the model above, the log-odds (logits) of RJA-BO is equal to the conditional mean (b_0), plus the unique effects of age (b_1), nonverbal IQ (b_2), diagnostic status (b_3), RJA-ET (b_4), age*RJA-ET interaction (b_5), nonverbal IQ*RJA-ET interaction (b_6), and diagnostic status*RJA-ET interaction (b_7).

Analysis #3 final model was as follows.

IJA-BO = b_0 + b_1*ZAge + b_2*ZNVIQ + b_3*Dxeff

+ b_4*ZIJA-ET

+ b_5*ZAge*ZIJA-ET + b_6*ZNVIQ*ZIJA-ET + b_7*Dxeff*ZIJA-ET

In the model above, IJA-BO is equal to the conditional mean (b_0), plus the unique effects of age (b_1), NVIQ (b_2), diagnostic status (b_3), IJA-ET (b_4), age*IJA-ET interaction (b_5), nonverbal IQ *IJA-ET interaction (b_6), and diagnostic status*IJA-ET interaction (b_7).

CHAPTER 4: RESULTS

Preliminary Analyses

Descriptive statistics. Table 2 presents the means and standard deviations for participants' age, verbal and nonverbal IQ, adaptive functioning, and autism symptomatology, by group. Additionally, Table 3 presents descriptive statistics for each eye-tracking variable by group, and Tables 4-9 present the zero-order correlations among predictor and outcome variables for each analysis. There were no significant zero-order correlations among eye-tracking variables (rs = -0.01 – 0.08, ps = 0.623 – 0.932).

Missing data. Three participants were excluded from all analyses due to poor eye-tracking (N = 1) or nonverbal IQ (N = 2) data quality. Several participants were excluded from at least one analysis due to poor data quality: eye-tracking response to joint attention (N = 1) and eye-tracking initiation of joint attention (N = 2).

Video coding reliability. Following the training period, interrater reliability between the principal investigator and secondary coder was greater than 80% on for each variable on each of the three reliability checks.

Table 2.
Participant Characteristics

	ASD			TYP					
	N	*M*	*(SD)*	*N*	*M*	*(SD)*	*df*	*t*	*p*
Sex, F/M	7/13			9/13					0.758
Age (months)	20	45.55	(13.51)	22	46.14	(14.08)	40	-0.137	0.891
NVIQ	19	30.26	(8.96)	21	53.86	(8.12)	38	-8.740	<0.001
VIQ	19	31.58	(12.94)	18	54.61	(9.29)	35	-6.187	<0.001
VABS ABC	19	69.89	(14.99)	22	107.18	(9.11)	29	-9.441	<0.001
ADOS CSS SA	20	6.70	(2.03)	22	1.86	(1.52)	40	8.792	<0.001
ADOS CSS RRB	20	6.60	(2.19)	22	2.50	(2.28)	40	5.930	<0.001
ADOS CSS Total	20	6.70	(2.11)	22	1.64	(1.43)	33	9.024	<0.001
SCQ Lifetime	19	17.84	(6.07)	20	5.10	(3.58)	29	7.935	<0.001
SCQ Current	19	15.58	(5.83)	20	3.75	(3.13)	27	7.834	<0.001
ADI-R A	18	15.78	(6.75)	--	--	--	--	--	--
ADI-R B	18	10.67	(4.63)	--	--	--	--	--	--
ADI-R C	18	5.33	(2.33)	--	--	--	--	--	--
ADI-R D	18	4.00	(0.91)	--	--	--	--	--	--

Note. ASD = Autism Spectrum Disorder; TYP = typically developing controls; F = female; M = male; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning Visual Reception and Fine Motor T-score average; VIQ = verbal intelligence quotient, as measured by Mullen Scales of Early Learning Receptive and Expressive Language T-score average; VABS ABC = Vineland Adaptive Behavior Scales, Third Edition, Adaptive Behavior Composite; ADOS CSS = Autism Diagnostic Observation Scale, Second Edition, Calibrated Severity Scale; SA = social affect; RRB = restricted or repetitive behavior; SCQ = Social Communication Questionnaire; ADI-R = Autism Diagnostic Interview, Revised.

Table 3.
Descriptive Statistics of Eye Tracking Variables by Group

	ASD				TYP			
	N	*M*	*(SD)*	*Range*	*N*	*M*	*(SD)*	*Range*
SocGeoPref-ET	19	0.53	(0.20)	0.16-0.90	22	0.55	(0.17)	0.13-0.92
RJA-ET	18	0.48	(0.33)	0.00-1.00	22	0.65	(0.27)	0.00-1.00
IJA-ET	17	1.89	(1.30)	0.33-4.33	22	1.74	(1.25)	0.00-5.50

Note. ASD = Autism Spectrum Disorder; TYP = typically developing controls; SocGeoPref-ET = Social Geometric Preferential Looking Eye-Tracking Task, percentage of time spent looking at social scene; RJA-ET = Response to Joint Attention Eye-Tracking Task, percentage of valid trials with accurate first gaze shifts; IJA-ET = Initiation of Joint Attention Eye-Tracking Task, number of transitions between face and target object per valid trial.

Main Analyses

Prior to all analyses, dependent variables were assessed for assumptions of normality, linearity, and homogeneity of variance. Inspection of histograms, P-P plots, and residual plots found assumptions were met for all dependent variables. Continuous variables were converted into *z* scores and categorical independent variables were effect coded for ease of interpretation. Additionally, data were examined for the possible presence of any outliers. Two scores surpassed the two-standard deviation threshold, indicating possible outliers. Analyses were performed with and without the possible outliers, which indicated no major changes to results when the cases were excluded. Correlations were first examined to assess for multicollinearity. No predictor-predictor relationships exceeded r = +/- 0.90; however, diagnostic status and nonverbal IQ variables were highly correlated (r = -0.80 to -0.84).[1]

Aim 1.

Basic visual social attention. Mean scores, standard deviations, and number of participants with valid scores are reported in Tables 3 and 4a. Multiple linear regression with sequential predictor entry was used to predict percentage of time spent looking at social scenes (Table 4b). Results showed that age and nonverbal IQ, which comprised the first block, did not account for significant variation, R^2 = 0.15 ($R^2_{adjusted}$ = 0.10), $F(2,36) = 3.11$, p = 0.057. Controlling for age and nonverbal IQ, the main effects of diagnosis (in Block 2) did not account for significant variance in percentage of time spent looking at social scene, R^2_{change} = 0.01, $F_{change}(1,35) = 0.41$, p = 0.526 (R^2_{total} = 0.16 and $R^2_{adjusted}$ = 0.09). In the third block, the

[1] Models were re-analyzed without nonverbal IQ and interaction terms, and results yielded no substantial differences from the original models.

interaction terms did not account for significant variation above and beyond age, nonverbal IQ, and diagnosis, $R^2_{change} = 0.12$, $F_{change}(4,31) = 1.28$, $p = 0.298$ ($R^2_{total} = 0.28$ and $R^2_{adjusted} = 0.11$).

Results from the final block, with all predictors entered in the model, showed that the average percentage of time spent looking at social scene was 56.69%, holding all other variables constant, $t(31) = 19.36$, $p < 0.001$. Age uniquely predicted percentage of time spent looking at social scene, with younger participants looking longer than older participants, $b = -12.18\%$, $SE = 4.13\%$, $t(31) = -2.95$, $p = 0.006$, $sr^2 = 0.21$ (see Figure 1). Specifically, for every standard deviation increase in age, percentage of time spent looking at social scene was predicted to decrease by 12.18%, holding all else constant. However, nonverbal IQ and diagnosis (see Figure 2) did not uniquely predict percentage of time spent looking at social scene (slope coefficient *t*-test *p*s = 0.396 and 0.730, respectively). Finally, there were no significant interactions between diagnosis and age; diagnosis and nonverbal IQ; and age and nonverbal IQ; or diagnosis, age, and nonverbal IQ (slope coefficient *t*-test *p*s = 0.471, 0.808, and 0.839, respectively). There was trend toward significance in the diagnosis, age, and nonverbal IQ interaction, $b = -10.75\%$, $SE = 5.31\%$, $t(31) = -2.03$, $p = 0.052$, $sr^2 = 0.10$.

Table 4a.
Correlation Table for Linear Regression using Sequential Predictor Entry - Social-Geometric Preferential Looking Eye-Tracking Task

Measure	*M*	*(SD)*	SocGeoPref-ET	Age	NVIQ	Diagnosis	Diagnosis* Age	Diagnosis* NVIQ	Age* NVIQ	Diagnosis* Age*NVIQ
Outcomes										
1. SocGeoPref-ET	0.55	(0.19)	--							
Block 1 Predictors										
2. Age	-0.09	(0.95)	-.35 *	--						
3. NVIQ	0.04	(0.98)	.17	-.03	--					
Block 2 Predictors										
4. Diagnosis	-0.08	(1.01)	-.07	-.02	-.81 ***	--				
Block 3 Predictors										
5. Diagnosis*Age	-0.01	(0.96)	.18	-.05	.18	-.10	--			
6. Diagnosis*NVIQ	-0.79	(0.57)	-.03	.16	.03	-.04	-.08	--		
7. Age*NVIQ	-0.04	(0.80)	-.11	.05	-.27 *	.20	-.72 ***	.02	--	
8. Diagnosis*Age*NVIQ	0.16	(0.78)	.03	-.72 ***	.04	-.03	.06	-.19	-.11	--

Note. N=39. SocGeoPref-ET = Social Geometric Preferential Looking Eye-Tracking Task, percentage of time spent looking at social scene; Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control.
* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 4b.

Multiple Linear Regression with Sequential Predictor Entry for Social-Geometric Preferential Looking Eye-Tracking Task

	Block 1					Block 2					Block 3				
	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2
Model Fit	0.15	0.15	0.10			0.01	0.16	0.09			0.12	0.28	0.11		
Coefficients															
Intercept				0.54 ***					0.54 ***					0.55 ***	
Age				-0.07 *	0.12				-0.07 *	0.11				-0.13 **	0.21
NVIQ				0.03	0.03				0.06	0.03				0.04	0.02
Diagnosis									0.03	0.01				0.02	0.00
Diagnosis*Age														0.04	0.02
Diagnosis*NVIQ														0.00	0.00
Age*NVIQ														0.01	0.00
Diagnosis*Age*NVIQ														-0.11	0.10

Note. N=39. Block 1 *F*-change test *df* = 2, 36; Block 2 *df* = 1, 35; Block 3 *df* = 4, 31. Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control. Results were substantively the same with robust standard errors; hence, results with regular standard errors are reported.

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

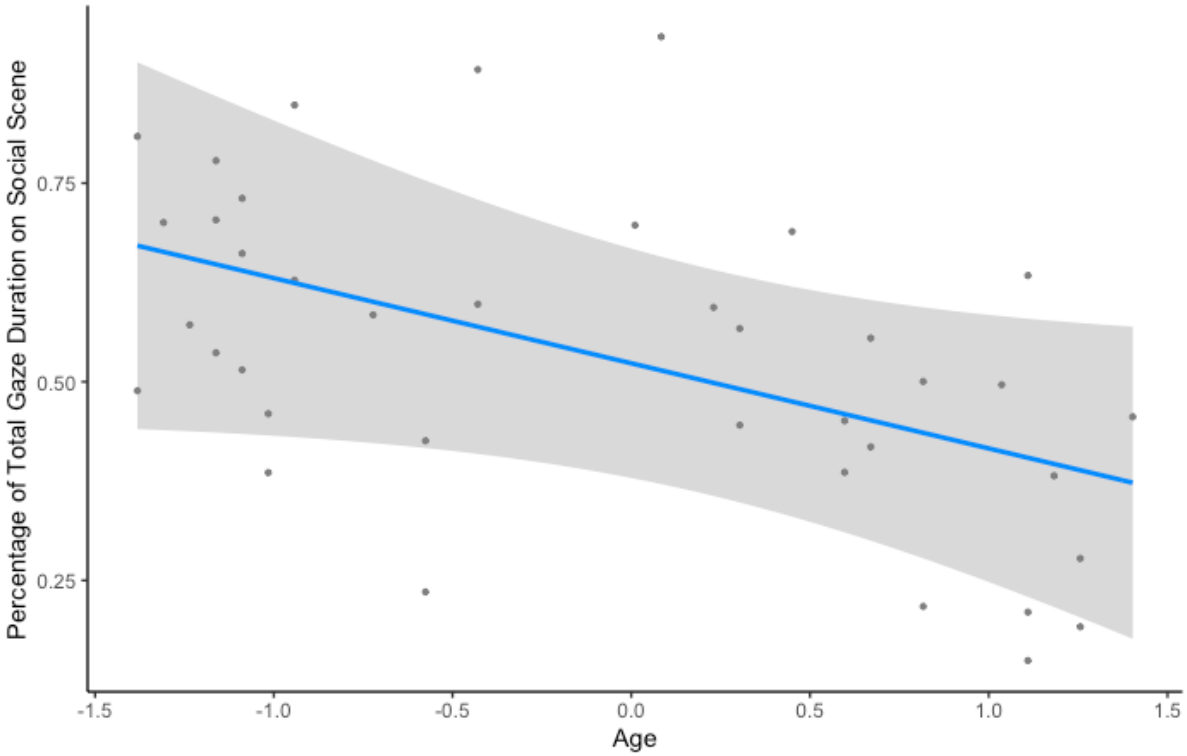

Figure 1. Relationship between age and percentage of total gaze duration on social scene, controlling for diagnosis, nonverbal IQ, and interaction effects. Significant main effect of age.

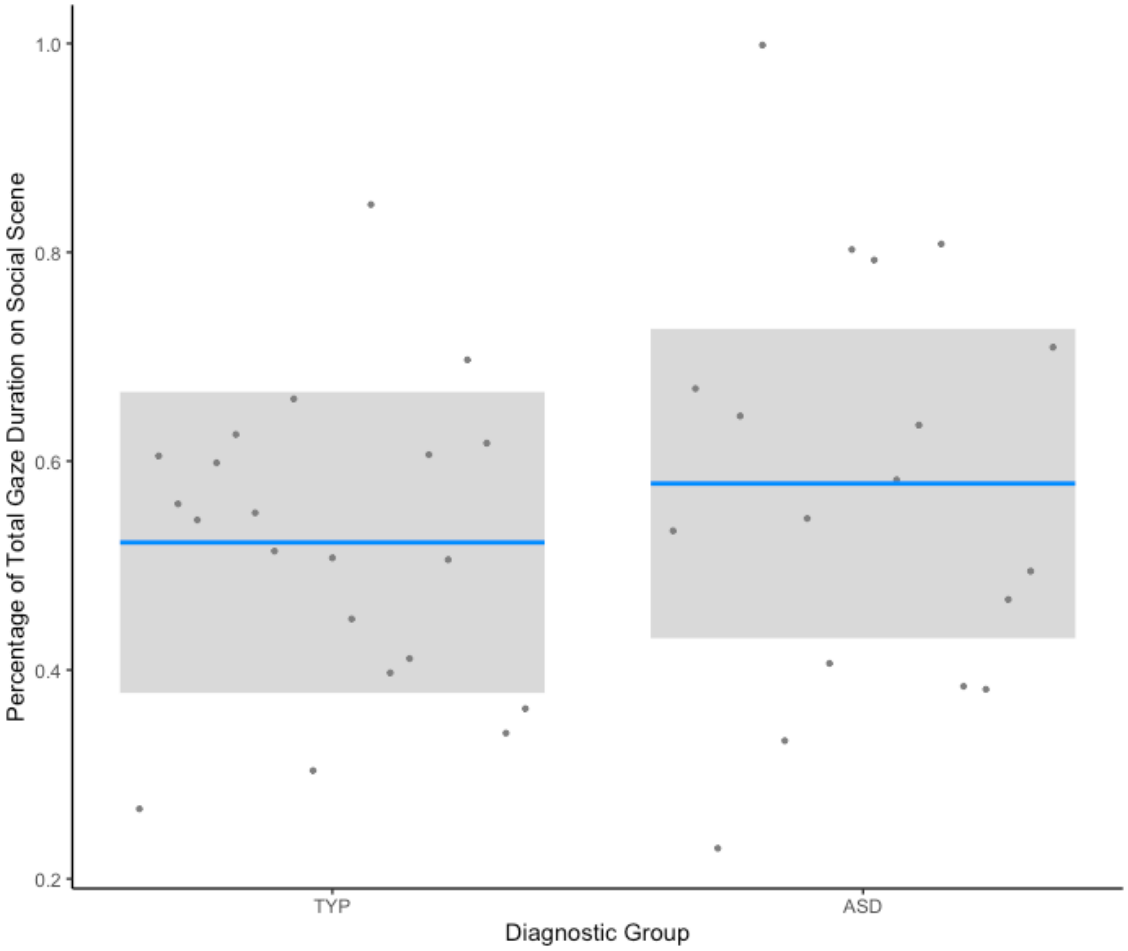

Figure 2. Percentage of total gaze duration on social scene by diagnostic group, controlling for age, nonverbal IQ, and interaction effects. No significant difference between groups.

Response to joint attention. Mean scores, standard deviations, and number of participants with valid scores are reported in Table 3 and 5a. Multiple linear regression with sequential predictor entry was used to predict percentage accurate gaze shifts (Table 5b). Results showed that age and nonverbal IQ, which comprised the first block, did not account for significant variation, $R^2 = 0.10$ ($R^2_{adjusted} = 0.05$), $F(2,35) = 1.98$, $p = 0.154$. Controlling for age and nonverbal IQ, the main effects of diagnosis (in Block 2) did not account for significant variance in percentage accurate gaze shifts, $R^2_{change} < 0.001$, $F_{change}(1,34) = 0.17$, $p = 0.896$ ($R^2_{total} = 0.10$ and $R^2_{adjusted} = 0.02$). In the third block, the interaction terms did not account for significant variation above and beyond age, nonverbal IQ, and diagnosis, $R^2_{change} = 0.04$, $F_{change}(4,30) = 0.33$, $p = 0.853$ ($R^2_{total} = 0.14$ and $R^2_{adjusted} = -0.06$).

Results from the final block, with all predictors entered in the model, showed that the average percentage accurate gaze shifts was 51.31%, holding all other variables constant, $t(30) = 5.68$, $p < 0.001$. Age, nonverbal IQ, and diagnosis (see Figure 3) did not uniquely predict percentage of accurate gaze shifts (slope coefficient *t*-test *p*s = 0.995, 0.228, and 0.901, respectively). Finally, there were no significant interactions among variables (slope coefficient *t*-test *p*s > 0.400).

Table 5a.
Correlation Table for Linear Regression using Sequential Predictor Entry - Response to Joint Attention Eye-Tracking Task

Measure	*M*	*(SD)*	RJA-ET	Age	NVIQ	Diagnosis	Diagnosis* Age	Diagnosis* NVIQ	Age* NVIQ	Diagnosis* Age*NVIQ
Outcomes										
1. RJA-ET	0.57	(0.31)	--							
Block 1 Predictors										
2. Age	-0.12	(0.95)	-.04	--						
3. NVIQ	0.08	(0.96)	.32 *	.01	--					
Block 2 Predictors										
4. Diagnosis	-0.11	(1.01)	-.07	-.05	-.81 ***	--				
Block 3 Predictors										
5. Diagnosis*Age	-0.03	(0.96)	.09	-.07	.22	-.13	--			
6. Diagnosis*NVIQ	-0.77	(0.57)	-.15	.20	-.03	.00	-.05	--		
7. Age*NVIQ	0.00	(0.78)	-.03	.10	-.36 *	.26	-.72 ***	-.04	--	
8. Diagnosis*Age*NVIQ	0.20	(0.75)	.03	-.71 ***	-.04	.02	.11	-.27 *	-.21	--

Note. N=38. RJA-ET = Response to Joint Attention Eye-Tracking Task, percentage of valid trials with accurate first gaze shifts; Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control.
* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 5b.

Multiple Linear Regression with Sequential Predictor Entry for Response to Joint Attention Eye-Tracking Task

	Block 1					Block 2					Block 3				
	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2
Model Fit	0.10	0.10	0.05			0.00	0.10	0.02			0.04	0.14	-0.06		
Coefficients															
Intercept				0.56 ***					0.05 ***					0.51 ***	
Age				-0.01	0.00				0.05	0.00				0.00	0.00
NVIQ				0.10	0.00				0.09	0.03				0.11	0.03
Diagnosis									0.09	0.00				-0.01	0.00
Diagnosis*Age														0.05	0.01
Diagnosis*NVIQ														-0.06	0.01
Age*NVIQ														0.09	0.02
Diagnosis*Age*NVIQ														0.02	0.00

Note. N=38. Block 1 *F*-change test *df* = 2, 35; Block 2 *df* = 1, 34; Block 3 *df* = 4, 30. Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control. Results were substantively the same with robust standard errors; hence, results with regular standard errors are reported.

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

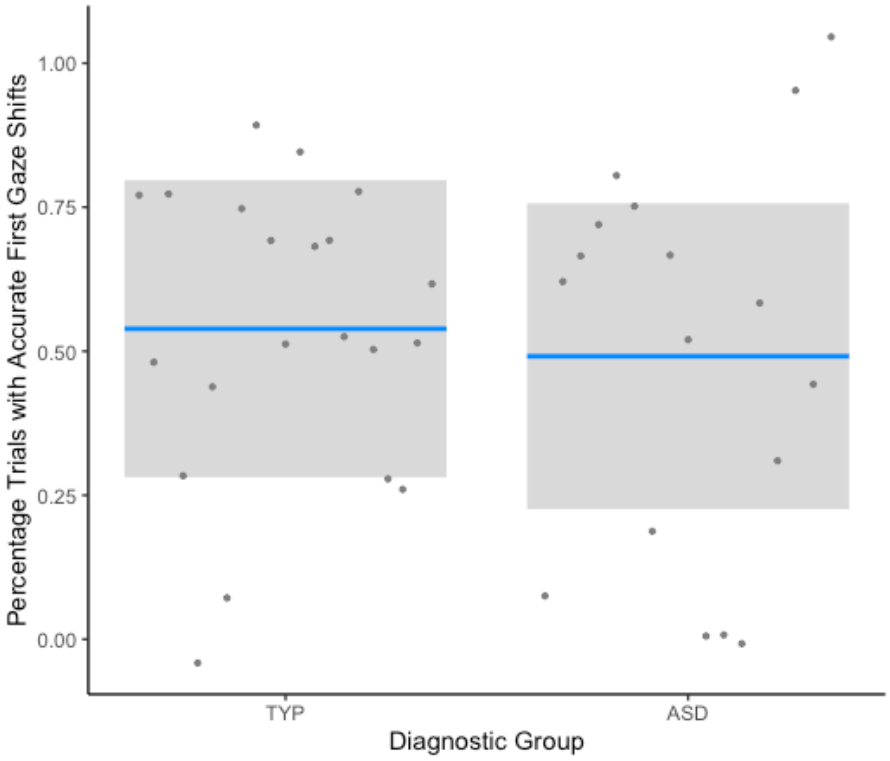

Figure 3. Percentage of total usable trials with congruent first gaze shifts by diagnostic group, controlling for age, nonverbal IQ, and interaction effects. No significant difference between groups.

Initiation of joint attention. Mean scores, standard deviations, and number of participants with valid scores are reported in Tables 3 and 6a. Multiple linear regression with sequential predictor entry was used to predict average number of transitions between face and target object (Table 6b). Results showed that age and nonverbal IQ, which comprised the first block, did not account for significant variation, $R^2 = 0.05$ ($R^2_{adjusted} = 0.01$), $F(2,34) = 0.88$, $p = 0.425$. Controlling for age and nonverbal IQ, the main effects of diagnosis (in Block 2) accounted for significant variance in average number of transitions between face and target object, $R^2_{change} < 0.19$, $F_{change}(1,33) = 8.15$, $p = 0.007$ ($R^2_{total} = 0.24$ and $R^2_{adjusted} = 0.17$). In the third block, the interaction terms did not account for significant variation above and beyond age, nonverbal IQ, and diagnosis, $R^2_{change} = 0.03$, $F_{change}(4,29) = 0.24$, $p = 0.912$ ($R^2_{total} = 0.26$ and $R^2_{adjusted} = 0.08$).

Results from the final block, with all predictors entered in the model, showed that the average number of transitions between face and target object was 2.11, holding all other variables constant, $t(29) = 6.29$, $p < 0.001$. Age did not uniquely predict average number of transitions between face and target object (slope coefficient t-test $p = 0.525$). However, nonverbal IQ and diagnosis (see Figure 4) each uniquely predicted average number of transitions between face and target object, $b = 1.10$ $SE = 0.37$, $t(29) = 2.97$, $p = 0.006$, $sr^2 = 0.22$; $b = 0.92$, $SE = 0.34$, $t(29) = 2.74$, $p = 0.010$, $sr^2 = 0.19$, respectively. Finally, there were no significant interactions among variables (slope coefficient t-test ps > 0.400).

Table 6a.
Correlation Table for Linear Regression using Sequential Predictor Entry - Initiation of Joint Attention Eye-Tracking Task

Measure	*M*	*(SD)*	IJA-ET	Age	NVIQ	Diagnosis	Diagnosis* Age	Diagnosis* NVIQ	Age* NVIQ	Diagnosis* Age*NVIQ
Outcomes										
1. IJA-ET	1.88	(1.25)	--							
Block 1 Predictors										
2. Age	-0.09	(0.95)	.08	--						
3. NVIQ	0.11	(0.95)	.20	-.02	--					
Block 2 Predictors										
4. Diagnosis	-0.14	(1.00)	.09	-.02	-.80 ***	--				
Block 3 Predictors										
5. Diagnosis*Age	-0.01	(0.96)	.09	-.10	.20	-.10	--			
6. Diagnosis*NVIQ	-0.76	(0.57)	.11	.20	-.04	.01	-.07	--		
7. Age*NVIQ	-0.03	(0.77)	-.04	.14	-.34 *	.23	-.71 ***	-.03	--	
8. Diagnosis*Age*NVIQ	0.18	(0.75)	-.09	-.71 ***	-.01	-.01	.15	-.27	-.25	--

Note. N=37. IJA-ET = Initiation of Joint Attention Eye-Tracking Task, number of transitions between face and target object per valid trial; Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control.
* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 6b.

Multiple Linear Regression with Sequential Predictor Entry for Initiation of Joint Attention Eye-Tracking Task

	Block 1					Block 2					Block 3				
	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2
Model Fit	0.05	0.05	-0.01			0.19 **	0.24	0.17			0.03	0.26	0.08		
Coefficients															
Intercept				1.86 ***					1.90 ***					2.11 ***	
Age				0.11	0.01				0.15	0.01				0.19	0.01
NVIQ				0.27	0.04				1.03 **	0.22				1.10 **	0.22
Diagnosis									0.90 **	0.19				0.92 **	0.19
Diagnosis*Age														0.16	0.01
Diagnosis*NVIQ														0.31	0.02
Age*NVIQ														0.27	0.01
Diagnosis*Age*NVIQ														0.16	0.00

Note. N=37. Block 1 *F*-change test *df* = 2, 34; Block 2 *df* = 1, 33; Block 3 *df* = 4, 29. Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control. Results were substantively the same with robust standard errors; hence, results with regular standard errors are reported.

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

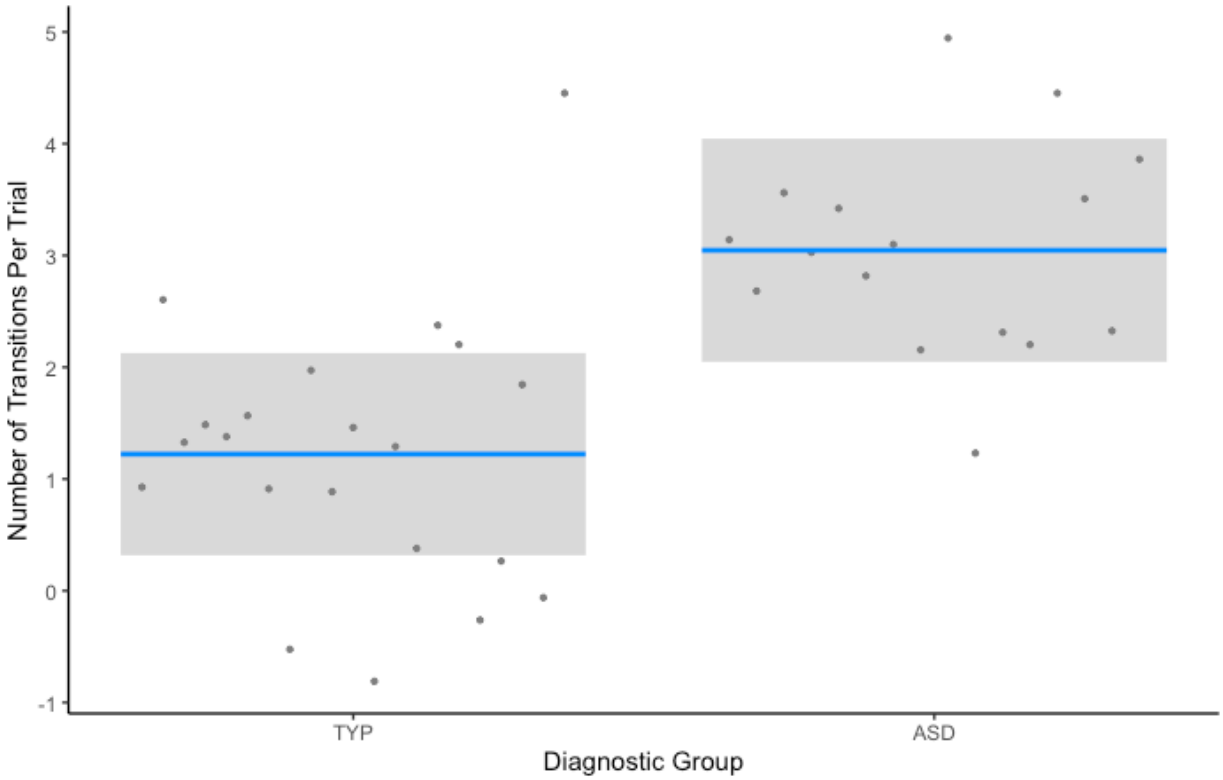

Figure 4. Average number of transitions between target object and face per valid trial by diagnostic group on the Initiation of Joint Attention paradigm, controlling for age, nonverbal IQ, and interaction effects. Significant difference between groups.

Aim 2.

Basic visual social attention. Multiple linear regression with sequential predictor entry was used to predict SOC-RS Social Referencing (Table 7b). Results showed that diagnosis, age and nonverbal IQ, which comprised the first block, accounted for significant variation, $R^2 = 0.36$ ($R^2_{adjusted} < 0.30$), $F(3,35) = 6.52$, $p = 0.001$. Controlling for diagnosis, age, and nonverbal IQ, the main effects of percentage of time spent looking at social scene during eye-tracking (in Block 2) accounted for significant variance in SOC-RS Social Referencing, $R^2_{change} = 0.07$, $F_{change}(1,34) = 4.17$, $p = 0.049$ ($R^2_{total} = 0.43$ and $R^2_{adjusted} = 0.36$). In the third block, the interaction terms did not account for significant variation above and beyond age and eye-tracking looking time at social scene, $R^2_{change} = 0.08$, $F_{change}(3,31) = 1.68$, $p = 0.19$ ($R^2_{total} = 0.51$ and $R^2_{adjusted} = 0.40$).

Results from the final block, with all predictors entered in the model, showed that the average SOC-RS Social Referencing duration was 5.58 seconds per minute, holding all other variables constant, $t(31) = 11.67$, $p < 0.001$. Age and nonverbal IQ uniquely predicted SOC-RS social referencing duration (age: $b = 1.41$, $SE = 0.50$, $t(31) = 2.80$, $p = 0.009$, $sr^2 = 0.12$; nonverbal IQ: $b = 2.14$, $SE = 0.79$, $t(31) = 2.72$, $p = 0.011$, $sr^2 = 0.12$; see Figure 5). Diagnostic status did not uniquely predict SOC-RS social referencing duration (slope coefficient t-test $p = 0.662$). Importantly, eye-tracking social looking time uniquely predicted SOC-RS social referencing duration, with participants with longer eye-tracking social looking times having longer SOC-RS social referencing duration, $b = 1.31$, $SE = 0.50$, $t(31) = 2.60$, $p = 0.014$, $sr^2 = 0.11$ (see Figure 5). Specifically, for every standard deviation increase in eye-tracking social looking time, SOC-RS social referencing duration was predicted to increase by 1.31 seconds per minute, holding all else constant. Finally, there were no significant interactions between eye-

tracking social looking time and age, nonverbal IQ, or diagnostic status (slope coefficient *t*-test *p*s = 0.139, 0.132, and 0.336, respectively).

Table 7a.
Correlation Table for Linear Regression using Sequential Predictor Entry- SOC-RS Social Referencing

Measure	*M*	*(SD)*	SocRef-BO	Age	NVIQ	Diagnosis	SocGeoPref-ET	SocGeoPref-ET *Age	SocGeoPref-ET *NVIQ	SocGeoPref-ET *Diagnosis
Outcomes										
1. SocRef-BO	5.42	(3.46)	--							
Block 1 Predictors										
2. Age	-0.09	(0.95)	.22	--						
3. NVIQ	0.04	(0.98)	.54 ***	-.03	--					
4. Diagnosis	-0.08	(1.01)	-.40 **	-.02	-.81 ***	--				
Block 2 Predictors										
5. SocGeoPref-ET	0.03	(1.01)	.26	-.35 *	.17	-.07	--			
Block 3 Predictors										
6. SocGeoPref-ET*Age	-0.33	(0.83)	.12	-.11	-.10	.18	-.01	--		
7. SocGeoPref-ET*NVIQ	0.17	(1.00)	.04	-.08	-.03	-.03	-.28 *	.12	--	
8. SocGeoPref-ET*Diagnosis	-0.07	(1.01)	-.01	.18	-.04	.03	.06	-.16	-.76 ***	--

Note. N=39. SOC-RS = Social Orienting Continuum and Response Scale; SocRef-BO = SOC-RS Social Referencing Behavioral Observation; Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control; SocGeoPref-ET = Social Geometric Preferential Looking Eye-Tracking Task, percentage of time spent looking at social scene, standardized.
* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 7b.

Multiple Linear Regression with Sequential Predictor Entry for SOC-RS Social Referencing

	Block 1					Block 2					Block 3				
	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2
Model Fit	0.36 ***	0.36	0.30			0.07 *	0.43	0.36			0.08	0.51	0.40		
Coefficients															
Intercept				5.45 ***					5.45 ***					5.57 ***	
Age				0.89	0.06				1.24 *	0.10				1.41 **	0.12
NVIQ				2.41 **	0.16				2.11 *	0.12				2.14 *	0.12
Diagnosis				0.57	0.01				0.40	0.00				0.34	0.00
SocGeoPref-ET									0.98 *	0.07				1.31 *	0.11
SocGeoPref-ET*Age														0.82	0.04
SocGeoPref-ET*NVIQ														1.14	0.04
SocGeoPref-ET*Diagnosis														0.68	0.02

Note. N=39. Block 1 *F*-change test *df* = 3, 35; Block 2 *df* = 1, 34; Block 3 *df* = 3, 31. SOC-RS = Social Orienting Continuum and Response Scale; Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control; SocGeoPref-ET = Social Geometric Preferential Looking Eye-Tracking Task, percentage of time spent looking at social scene, standardized. Results were substantively the same with robust standard errors; hence, results with regular standard errors are reported.

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

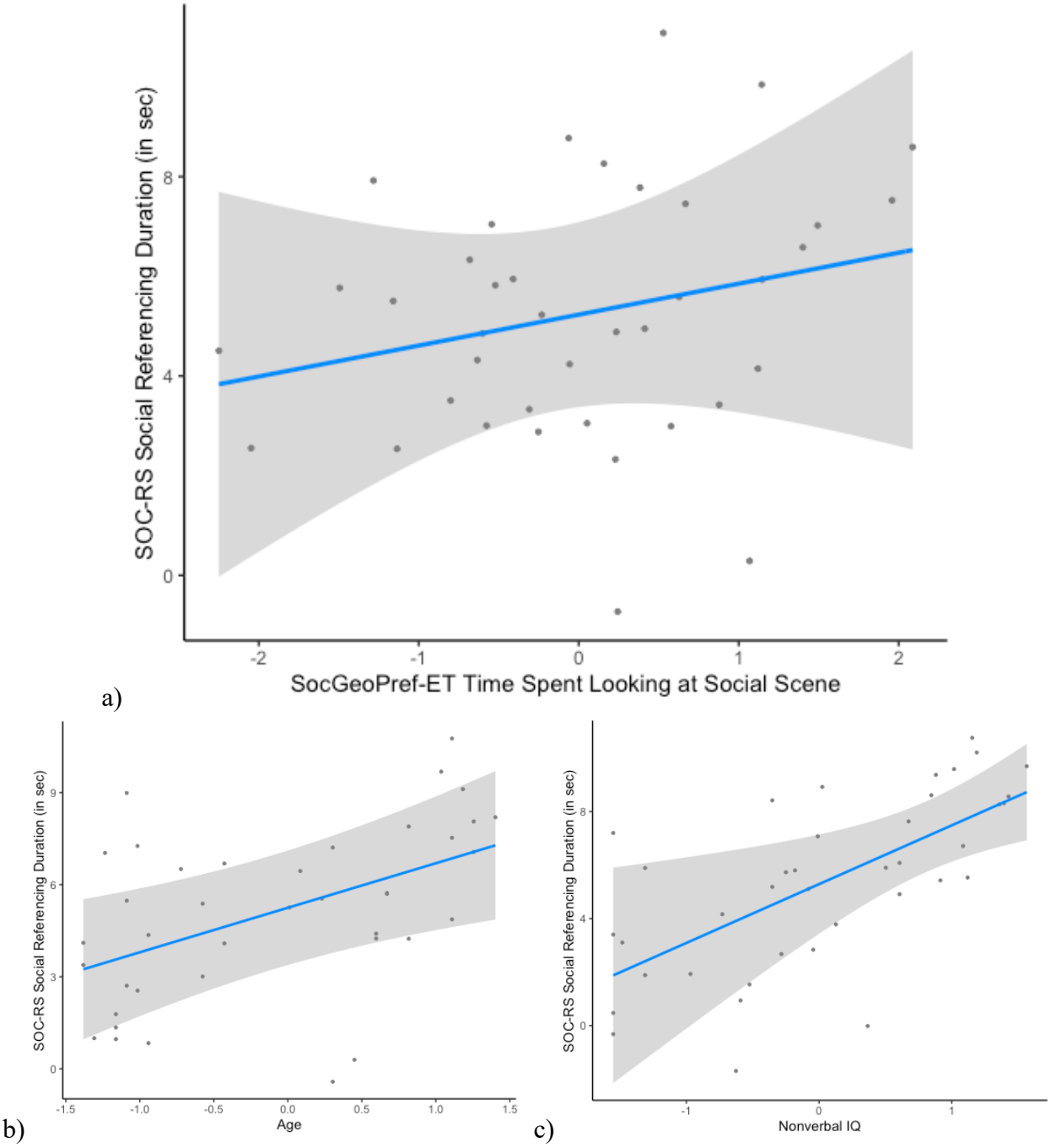

Figure 5. Average duration (in seconds) of social referencing per minute of observable time by a) percentage of total gaze duration on social scenes in the SocGeoPref eye-tracking task, b) age, and c) nonverbal IQ, controlling for other main and interaction effects. Significant main effects for eye-tracking gaze duration, age, and nonverbal IQ.

Response to joint attention. A multiple logistic regression with sequential predictor entry was used to predict SOC-RS Response to Joint Attention using a sample of $N = 22$ preschool children (Table 8b). Age, gender, and diagnosis were entered in Block 1 and together were found to have a better model fit than the null model with no predictors, $\chi^2(3) = 9.39$, $p = 0.025$. The approximate variance in SOC-RS Response to Joint Attention accounted for was 0.503 using Nagelkerke's formula, and model sensitivity was 75% and specificity was 83% (the overall hit rate was 77%, which was slightly better than the null model's hit rate of 73%).

In Block 2, eye-tracking percentage of congruent first gaze shifts was entered into the model and was not found to have a better fit than the model with Age, gender, and diagnostic status alone, $\chi^2(1) = 2.77$, $p = 0.096$. Nevertheless, the overall model fit was still significantly better than the null $\chi^2(4) = 12.16$, $p = 0.016$. The model's Nagelkerke's pseudo-$R^2 = 0.62$, and sensitivity and specificity were 94% and 67%, respectively. The overall hit rate was 86%, which was better than the hit rate for the model with age, gender, and diagnostic status alone (77%).

Finally, in Block 3, which included interaction terms, was not significant, $\chi^2(3) = 0.373$, $p = 0.946$. The overall model fit was no longer significantly better than the null $\chi^2(7) = 12.53$, $p = 0.084$ (overall hit rate remained the same at 86%). As shown in Figure 6, there was a trend for participants with a higher percentage of accurate gaze shifts to respond to an eye-gaze-only bid for joint attention (SOC-RS RJA).

For brevity, only the coefficient estimates from the final model with all predictors entered is interpreted here. Model results showed that the intercept was not significantly different from zero (or in other words, the mean predicted probability was not significantly different from

50%): the log-odds of SOC-RS Response to Joint Attention across the sample (holding all predictors constant) was $b = 11.91$ ($SE = 6774.57$), $Wald(1) < 0.01$, $p = 0.99$.

None of the predictors were uniquely predictive of SOC-RS RJA: age, $b = 1.24$ ($SE = 1.58$), $Wald(1) = 0.61$, $p = 0.434$; nonverbal IQ, $b = 0.539$ ($SE = 1.40$), $Wald(1) = 0.15$, $p = 0.701$; diagnostic status, $b = -10.22$ ($SE = 6774.57$), $Wald(1) < 0.01$, $p = 0.999$; eye-tracking RJA, $b = 0.37$ ($SE = 7777.53$), $Wald(1) < 0.01$, $p > 0.999$; eye-tracking*age, $b = -0.08$ ($SE = 2.31$), $Wald(1) < 0.01$, $p = 0.971$; eye-tracking*nonverbal IQ, $b = -0.80$ ($SE = 2.13$), $Wald(1) = 0.14$, $p = 0.705$; and eye-tracking*diagnosis, $b = -0.02$ ($SE = 7777.53$), $Wald(1) <0.01$, $p > 0.999$.

Table 8a.
Correlation Table for Logistic Regression using Sequential Predictor Entry- SOC-RS Response to Joint Attention

Measure	*M*	*(SD)*	RJA-BO	Age	NVIQ	Diagnosis	RJA-ET	RJA-ET *Age	RJA-ET *NVIQ	RJA-ET *Diagnosis
Outcomes										
1. RJA-BO	0.73	(0.46)	--							
Block 1 Predictors										
2. Age	-0.77	(0.60)	.01	--						
3. NVIQ	-0.11	(1.04)	.46 *	-.24	--					
4. Diagnosis	0.09	(1.02)	-.56 **	.14	-.84 ***	--				
Block 2 Predictors										
5. RJA-ET	-0.02	(1.04)	.48 *	-.15	.34	-.35	--			
Block 3 Predictors										
6. RJA-ET*Age	-0.08	(1.01)	-.36 *	.12	-.20	.26	-.80 ***	--		
7. RJA-ET*NVIQ	0.35	(0.88)	-.26	.16	.15	-.06	-.35	.08	--	
8. RJA-ET*Diagnosis	-0.35	(0.98)	.30	-.04	-.06	.01	.36	-.28	-.79 ***	--

Note. N=22. SOC-RS = Social Orienting Continuum and Response Scale; RJA-BO = SOC-RS Response to Joint Attention Behavioral Observation; Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control; RJA-ET = Response to Joint Attention Eye-Tracking Task, percentage of valid trials with accurate first gaze shifts, standardized.
* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 8b.

Multiple Logistic Regression with Sequential Predictor Entry for SOC-RS Response to Joint Attention

	Block 1					Block 2						Block 3					
	χ^2_{total}		*Nagel.*	*HR*	*b*	*OR*	χ^2_{change}	χ^2_{total}		*Nagel.*	*HR*	*b*	*OR*	χ^2_{change}	χ^2_{total}	*Nagel.*	*HR*	*b*	*OR*
Model Fit	9.39	*	0.50	77.30			2.77	12.16	*	0.62	86.40			0.37	12.53	0.63	86.40		
Coefficients																			
Intercept					11.04							11.47						11.91	
Age					0.54	1.71						0.91	2.49					1.24	3.46
NVIQ					0.16	1.18						0.33	1.39					0.54	1.71
Diagnosis					-10.52	0.00						-10.22	0.00					-10.22	0.00
RJA-ET												1.01	2.76					0.36	1.44
RJA-ET*Age																		-0.08	0.92
RJA-ET*NVIQ																		-0.80	0.45
RJA-ET*Diagnosis																		-0.02	0.98

Note. N=22. Block 1 chi-square change test *df* = 3; Block 2 *df* = 1; Block 3 *df* = 3. SOC-RS = Social Orienting Continuum and Response Scale; Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control; RJA-ET = Response to Joint Attention Eye-Tracking Task, percentage of valid trials with accurate first gaze shifts, standardized.

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

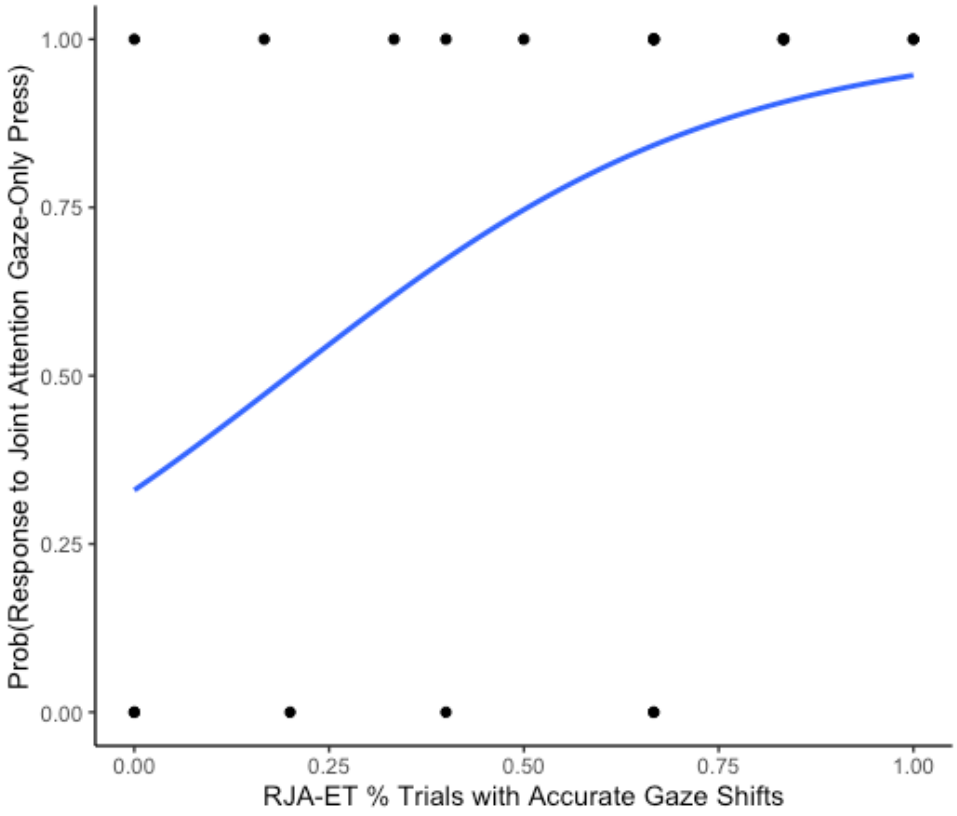

Figure 6. Probability of response on ADOS-2 gaze-only press given percentage of trials with accurate first gaze shifts on Response to Joint Attention eye-tracking task.

Initiation of joint attention. Multiple linear regression with sequential predictor entry was used to predict SOC-RS Initiation of Joint Attention (Table 9b). Results showed that diagnosis, age and nonverbal IQ, which comprised the first block, did not account for significant variation, $R^2 = 0.12$ ($R^2_{adjusted} = 0.04$), $F(3,32) = 1.49$, $p = 0.236$. Controlling for diagnosis, age, and nonverbal IQ, the main effects of average number of transitions between target object and face (in Block 2) did not account for significant variance in SOC-RS Initiation of Joint Attention, $R^2_{change} = 0.01$, $F_{change}(1,31) = 0.42$, $p = 0.522$ ($R^2_{total} = 0.13$ and $R^2_{adjusted} = 0.02$). In the third block, the interaction terms did not account for significant variation above and beyond age and eye-tracking average number of transitions between target object and face, $R^2_{change} = 0.02$, $F_{change}(3,28) = 0.24$, $p = 0.871$ ($R^2_{total} = 0.16$ and $R^2_{adjusted} = -0.06$).

Results from the final block, with all predictors entered in the model, showed that the average SOC-RS Initiation of Joint Attention was 0.41, holding all other variables constant, $t(28) = 5.54$, $p < 0.001$. Age, nonverbal IQ, diagnostic status, and eye-tracking average number of transitions between target object and face did not uniquely predict SOC-RS initiation of joint attention (slope coefficient *t*-test *p*s = 0.081, 0.872, 0.926, and 0.636). Furthermore, there were no significant interactions between eye-tracking average number of transitions between target object and face and age, nonverbal IQ, or diagnostic status (slope coefficient *t*-test *p*s = 0.539, 0.913, and 0.751, respectively).

Table 9a.
Correlation Table for Linear Regression using Sequential Predictor Entry- SOC-RS Initiation of Joint Attention

Measure	*M*	*(SD)*	IJA-BO	Age	NVIQ	Diagnosis	IJA-ET	IJA-ET *Age	IJA-ET *NVIQ	IJA-ET *Diagnosis
Outcomes										
1. IJA-BO	0.42	(0.35)	--							
Block 1 Predictors										
2. Age	-0.08	(0.96)	-.34 *	--						
3. NVIQ	0.07	(0.94)	.07	.00	--					
4. Diagnosis	-0.11	(1.01)	-.09	-.04	-.80 ***	--				
Block 2 Predictors										
5. IJA-ET	-0.02	(0.88)	-.17	.14	.09	.19	--			
Block 3 Predictors										
6. IJA-ET*Age	0.12	(0.89)	.05	.18	.04	.06	.09	--		
7. IJA-ET*NVIQ	0.07	(0.72)	-.02	.07	-.35 *	.22	.16	.02	--	
8. IJA-ET*Diagnosis	0.17	(0.86)	-.11	.06	.17	-.01	.13	-.08	-.80 ***	--

Note. N=36. SOC-RS = Social Orienting Continuum and Response Scale; IJA-BO = SOC-RS Initiation of Joint Attention Behavioral Observation; Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control; IJA-ET = Initiation of Joint Attention Eye-Tracking Task, number of transitions between face and target object per valid trial, standardized.
* $p < .05$, ** $p < .01$, *** $p < .001$.

Table 9b.

Multiple Linear Regression with Sequential Predictor Entry for SOC-RS Initiation of Joint Attention

	Block 1					Block 2					Block 3				
	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2	R^2_{change}	R^2_{total}	R^2_{adj}	*b*	sr^2
Model Fit	0.12	0.12	0.04			0.01	0.13	0.02			0.02	0.16	-0.06		
Coefficients															
Intercept				0.40 ***					0.40 ***					0.41 ***	
Age				-0.12 *	0.11				-0.12	0.10				-0.12	0.10
NVIQ				-0.01	0.00				0.02	0.00				0.02	0.00
Diagnosis				-0.04	0.00				-0.01	0.00				-0.01	0.00
IJA-ET									-0.05	0.01				-0.04	0.01
IJA-ET*Age														0.04	0.01
IJA-ET*NVIQ														-0.02	0.00
IJA-ET*Diagnosis														-0.04	0.00

Note. N=36. Block 1 *F*-change test *df* = 3, 32; Block 2 *df* = 1, 31; Block 3 *df* = 3, 28. SOC-RS = Social Orienting Continuum and Response Scale; Age standardized; NVIQ = nonverbal intelligence quotient, as measured by Mullen Scales of Early Learning, standardized; Diagnosis effect-coded with 1=ASD, -1=typically developing control; IJA-ET = Initiation of Joint Attention Eye-Tracking Task, number of transitions between face and target object per valid trial, standardized. Results were substantively the same with robust standard errors; hence, results with regular standard errors are reported.

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

CHAPTER 5: DISCUSSION

Extreme etiological and behavioral heterogeneity in ASD has resulted in difficulty determining optimal interventions for each child with ASD. Social attention eye-tracking measures may provide a theoretically valid, high resolution, accessible option for measuring child characteristics related to core symptoms of ASD. Further examination of the properties and construct validity of these eye-tracking measures provides foundational evidence regarding the utility of the eye-tracking measures as predictors of response to intervention. The main purposes of this study were to examine the properties of social attention eye-tracking measures in young children with ASD relative to typically developing peers, as well as to relate more ecological behavioral indicators of social attention to eye-tracking measures of social attention across basic visual social attention, response to joint attention, and initiation of joint attention.

Properties of Social Attention Eye-Tracking Measures

Basic Visual Social Attention. Although our study detected a wide range and variability of attention toward social scenes in the ASD group, similar range and variability were also found within the typically developing group. Not surprisingly, then, we failed to detect significant differences between the ASD and typically developing groups on percentage of time spent looking at social scenes, contrary to previous findings (e.g., Moore et al., 2018; Pierce et al., 2011). It is possible that inconsistent findings resulted from differences in participant characteristics. Our study included a wider age range of children (27-74 months) that skewed older than samples in Pierce and colleagues (2011; 2016), who studied toddlers, and Franchini and colleagues (2017), whose sample included children aged 14-57 months. In fact, there was a significant effect of age in our sample in that younger participants tended to look longer at dynamic social scenes than older participants. This finding is consistent with previous studies

(Franchini et al., 2017; Pierce et al., 2016), who have suggested that between group effects may be insignificant in children over 4 years old. With the small sample size in the current study, effects of diagnostic status may be undetected given great variability as a result of the age range. Restricting our sample to individuals under 4 years old increases diagnostic status R^2 from 0.003 to 0.05, and restricting our sample to individuals under 3 years old further increases diagnostic status R^2 to 0.24. Furthermore, the range of the percentage of looking time at social scenes for our sample under 4 years old paralleled that of previous studies for both ASD (range = 0.16-0.90) and typically developing (range = 0.46-0.92) groups. The large variability in the ASD group with a subset of scores non-overlapping with the typically developing group indicate good properties to parse heterogeneity in basic visual social attention for children under 4 years.

Along with sample age range, minor adjustments to stimuli presentation may have also contributed to the inconsistent findings. The original stimuli developed by Pierce and colleagues (2011) were presented for 60 seconds in total, whereas, our study presented stimuli for 128 seconds in total. It is possible that participants acclimated to stimuli given the longer presentation time, which may have altered looking patterns compared to previous studies. Pierce and colleagues (2011) noted a reduced magnitude of between-group differences and increased percentage of looking time to the geometric scenes in all groups over the course of the stimulus presentation. A recent meta-analysis indicated social content may also moderate group differences in social versus non-social preferential looking tasks (Chita-Tegmark, 2016). Although, Moore and colleagues (2018) have shown that the SocGeoPref-ET measure is robust to small changes in stimulus complexity (e.g., one versus two children in the social scene) in toddlers, it is possible that the complexity of social stimuli impacted looking patterns in the older participants in our sample. Modifying the stimuli in consideration of social complexity may

strengthen our ability to detect differences in looking patterns between groups of wider age ranges. Overall, our analyses confirmed effects of age on gaze behavior on the SocGeoPref-ET task and the necessity of considering social content and length of presentation. Nevertheless, when restricted to children under 4 years old, the SocGeoPref-ET task appears to hold adequate properties as a potential predictor of response to intervention.

Response to Joint Attention. The range of responses was similar in ASD and typically developing groups, and no mean differences were found between ASD and typically developing control participants on the eye-tracking measure of response to joint attention. Although one previous study (Falck-Ytter et al., 2012) found group differences in gaze accuracy on the response to joint attention paradigm, our findings are consistent with several other studies with samples including infants (Bedford et al., 2012), toddlers (Billeci et al., 2016), and preschool children (Falck-Ytter et al., 2015) that found no differences among groups in gaze accuracy. Failure to detect differences between groups in the eye-tracking measure of response to joint attention is not likely to reflect a lack of reduced response to joint attention in our ASD sample. Post hoc comparison of response to joint attention during the ADOS-2 revealed significant differences between groups in the real-world context (ADOS-2 RJA press; $p = 0.007$).

Differences in sample characteristics may account for discrepant findings. Falck-Ytter et al., (2012) grouped participants into Autistic Disorder (AD), Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS) and typically developing (TYP). They found differences in RJA accuracy between AD and TYP groups, but not between PDD-NOS and TYP groups. As AD represented individuals with more severe ASD symptoms prior to re-classification in the DSM-5, significant findings may be attributed to reduced heterogeneity in the AD group. Our

study and other previous studies grouped individuals with ASD into a single diagnostic status, adding to the heterogeneity within group and reducing probability of finding robust differences.

Although many studies found no diagnostic group differences in RJA accuracy, some studies did find differences between groups in duration of looking at the target or congruent object (lower duration in ASD) in infants and preschoolers, presumably representing limited processing bias in ASD (Bedford et al., 2012; Falck-Ytter et al., 2012). Our study measured RJA accuracy using percentage of valid trials with accurate first gaze shifts, as it has been preliminarily shown as the most measure most highly correlated with real-world RJA behavior in comparison to other measures (including difference score), particularly to a distal object (Navab et al., 2012). Most studies used difference score or normalized gaze transition score to represent RJA accuracy (Bedford et al., 2012; Billeci et al., 2016; Falck-Ytter et al., 2012; Falck-Ytter et al., 2015). Therefore, although our study did not find significant differences between ASD and typically developing groups, accuracy of first gaze shift may not be the most robust measure to differentiate between ASD and typically developing preschool age children. Other dimensions of gaze behavior may provide more utility, including duration of looking at the target object following an accurate gaze shift. These types of measures should be examined in relation to ecological behavioral measures of response to joint attention.

Initiation of Joint Attention. Regarding the initiation of joint attention paradigm, we found participants with ASD tended to make more transitions between face and target object relative to typically developing controls. Our results are consistent with Billeci and colleagues' (2016) findings with a toddler sample and extend the findings to preschool children. However, results are counterintuitive in that children with ASD have been shown to have impairments in initiation of joint attention; that is, on a group level, children with ASD make fewer transitions

between others' faces and objects of interest than typically developing children (Mundy et al., 2009). Therefore, the eye-tracking task likely captures a construct distinct from initiation of joint attention. Nevertheless, Billeci's (2016) task appears to be capturing a consistent, significantly different gaze pattern between ASD and typically developing young children. Analyses and considerations related to construct validity are further discussed below.

Construct Validity of Social Attention Eye-Tracking Measures

Basic Visual Social Attention. Although no group differences were detected, we did find that visual social attention measured using Pierce and colleagues' (2011) SocGeoPref-ET task predicted social referencing duration in a more ecological context. That is, children who looked more at social scenes during the eye-tracking paradigm also tended to look more at others in a naturalistic real-world context (i.e., ADOS-2 administration). Age and nonverbal IQ also uniquely predicted real-world social referencing duration. Controlling for those factors, social attention on the eye-tracking measure remained a significant predictor. Although previous studies have found a negative relationship between looking time at social scenes and autism symptom severity (e.g., Moore et al., 2018), our study is the first to establish preliminary construct validity of a basic visual social attention eye-tracking measure in relation to a real-world behavioral measure of basic visual social attention. With a wide range of variability among individuals with ASD and preliminary construct validity established, the SocGeoPref-ET task appears to be a promising measure to identify individual child characteristics that contribute to the effectiveness of a given intervention.

Response to Joint Attention. The overall model that included RJA-ET, age, nonverbal IQ, and diagnosis, had a correct classification hit rate of 86% and was a significantly better fit than the null model. However, performance on the RJA-ET task did not significantly uniquely

predict real-world response to gaze-only joint attention bids (SOC-RS RJA). This finding is inconsistent with the only previous study examining the construct validity of the response to joint attention eye-tracking paradigm in infants (Navab et al., 2012). Although we were unable to confirm group differences or construct validity, our analysis was limited to a subset of participants who were administered the RJA press during the ADOS-2 (i.e., ADOS-2 modules 1-2 or toddler module; $N = 22$), which limited our power to detect effects. However, the large effect size (OR = 2.76) indicates potential for construct validity to be established given a sufficient sample size.

Our utility of a dichotomous variable to measure ecological behavior of response to joint attention may have also limited our ability to detect effects. The previous study of construct validity (Navab et al., 2012) utilized more dimensional behavioral RJA variables as measured with the Early Social Communication Scales (ESCS; Mundy et al., 2003). Overall, although we could not confirm construct validity, our study suggests potential for construct validity to be established in preschool children with an increased sample size and use of dimensional ecological behavioral measures, such as the ESCS.

Initiation of Joint Attention. We found that the eye-tracking initiation of joint attention did not predict real-world initiation of joint attention behavior. This is result is not surprising, given the counterintuitive between-group results, and it is, therefore, unlikely that this paradigm may be used to predict initiation of joint attention behavior in real-world contexts. Overall, it appears that Billeci and colleagues' (2016) initiation of joint attention paradigm has poor construct validity and should not be utilized to measure joint attention. However, as noted earlier, the measure does capture a significant difference in gaze patterns between ASD and typically developing children, namely, the number of gaze transitions between a face and target

object. Pierce and colleagues (2016) found similar gaze behavior toward social stimuli in their preferential looking task: the subset of their ASD participants who preferred looking at the geometric scene showed an increased number of saccades when looking at social scenes and decreased number of saccades when looking at geometric scenes. Therefore, the increased number of transitions between face and target object may reflect a general reduced interest in the social scene presented in the IJA-ET task. Overall, our study refutes the utility of Billeci's (2016) IJA task as one representative of initiation of joint attention behavior in ASD or typically developing children. Until its construct is well-understood, the IJA measure may provide limited utility as a predictor of response to intervention.

Limitations and Future Directions

Our study should be considered in the context of a number of limitations. First, our small sample size limited significant findings and the number of possible analyses. For example, we were unable to control for cultural factors moderating social communication behavior, such as reduced eye contact as a sign of respect in some cultural groups. Furthermore, although our groups were matched by age and gender, participants were not matched on nonverbal IQ. As a result, our final sample included a limited overlapping range of nonverbal IQ scores between ASD and typically developing groups. In effect, interactions could not be fully examined. In addition, our study recruited a relatively wide age range. With a limited sample size, reducing the range of ages may have increased the power to detect group differences. Finally, although all individuals in the ASD group held a reported diagnosis of ASD, we were unable to apply strict ADOS-2 and ADI-R cut-off criteria to designate eligibility in the group for analyses due to limited resources. Therefore, our ASD sample may represent a relatively wide range of

symptomatology, reducing the probability of detecting significant differences between ASD and typically developing groups.

Future studies should utilize gaze contingent technology in developing eye-tracking paradigms for joint attention. These such paradigms may improve construct validity, particularly with initiation of joint attention. In addition, studies should examine the relationship between these eye-tracking measures of social attention and real-world object or toy interest. Thus far, moderators of intervention outcomes relate to object interest, and recent studies have shown aberrations in reward processing span social and nonsocial stimuli. We hypothesize that social attention will correlate positively with object interest. Furthermore, intervention studies should be completed utilizing the basic visual social attention and response to joint attention eye-tracking measures examined in this study as predictors of response to intervention. These measures will provide increased clarity in child characteristics that may be contributing to variation in fit of intervention. For instance, hypotheses regarding effective versus ineffective active ingredients of an intervention would be more well-defined with nuanced quantitative data on social referencing behavior.

Limitations with the social motivation theory must be addressed. Although neuroimaging evidence supports the involvement of reward-related neurocircuitry in visual social attention, RJA, and IJA, causal relations are unclear. Do reward processing deficits cause reduced visual social attention, or do other aspects of functioning result in lower visual social attention, and ultimately lower reward value of social stimuli? Social attention behavior must, therefore, be interpreted with caution, and alternative explanations for reduced social attention should be considered. For example, alternative hypotheses suggest that individuals with ASD show reduced social attention due to sensory hypersensitivity (Takarae & Sweeney, 2017) or aberrant

motor mechanisms (B. Johnson et al., 2012). Future studies should include additional variables to distinguish among these mechanisms. For example, increased saccadic error variability has been observed in a number of studies of individuals with ASD (e.g., B. Johnson et al., 2012; B. Johnson, Rinehart, White, Millist, & Fielding, 2013) and can be examined in conjunction with social attention eye-tracking measures to better understand the contribution of aberrant ocular motor mechanisms in social attention eye-tracking behavior.

Conclusion

Currently, many families face challenges accessing adequate early intervention services for their children with ASD. Discovering efficient and effective predictors of response to intervention may mitigate these challenges, as individualized recommendations occurring earlier in the evaluative process may prevent delays in receiving intervention and inefficient utility of resources. This study sought to determine the suitability of social attention eye-tracking measures as predictors of response to intervention. Of the eye-tracking measures assessed, the basic visual social attention measure provides the most promise regarding utility as a predictor of response to intervention for children under 4 years old. Using this method of measurement may provide a meaningful way to parse the phenotypic heterogeneity in ASD on the basis of a specific underlying difference in attending to the social world that is present in some, but not all, children with ASD. As a pre-test measure in intervention studies, this social attention eye-tracking measure may aid in determining which interventions are effective, the dosage of intervention needed, and/or the active ingredients in an intervention that are most beneficial to each child.

Based on the social motivation theory, we would hypothesize that individuals with lower social attention represent individuals with reward learning deficits and would show the most

limited gains in interventions based on operant conditioning. If the theory holds true, the question remains what solutions should exist for those with deficits in reward learning. Many of the NDBIs and other behavioral interventions specifically target reduced child motivation with an increased dosage approach. With these interventions, social attention measures may predict necessary dosage of treatment. However, the problem remains that a sizable number of children with ASD do not benefit substantively from existing early interventions. Still unclear is whether the subset of children with the most severe reward learning deficits are those that benefit least from operant conditioning-based behavioral interventions. If this is the case, consideration of an intervention drawing upon alternative learning strategies or environmental adaptations to achieve access to comparable quality of life. To answer these questions, continued examination of child characteristics as predictors is necessary in the context of intervention studies. Furthermore, as recent advances in the field illuminate etiological subtypes of ASD, the use of eye-tracking tools to link etiology to basic behavior mechanisms may lead to greater understanding and development of novel interventions targeting specific mechanisms.

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