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Identifying Neurocognitive Endophenotypes in ASD: A Multi-method, Family Study of Visual Perception and Attention

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Kritika Nayar, MS

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ABSTRACT

Background: The way in which one perceives their visual world (i.e., bottom-up visual perception) and what one pays attention to in their surroundings (i.e., top-down attention), are critical to uncovering underlying thoughts and cognitions, and impact how one operates in the social world. Individuals with autism spectrum disorder (ASD), a neurodevelopmental disorder, demonstrate a local visual processing bias (i.e., tendency to perceive details) and social attention atypicalities (i.e., showing reduced attention allocated towards social information) compared to controls, which have been shown to relate to clinical-behavioral features of the disorder. As such, differences in visual perception and social attentional styles may be contributing to increased autism severity, suggesting a possible underlying biological mechanism related to ASD. Such differences in visual attention and perception have also been implicated more subtly in parents of individuals with ASD, suggesting a potential genetic influence on visual perception/attention. However, prior studies involving parents do not assess local/global visual processing explicitly nor do they comprehensively examine dynamic looking patterns of social attention, which are critical to uncovering processing strategies that may be contributing to clinical and sub-clinical ASD-related features. As such, the extent to which visual perception/attention constitute endophenotypes (i.e., measurable intermediate traits with closer ties to underlying biology) and whether differences are linked to underlying neurobiology, remains unknown. Because endophenotypes can be linked to observed behavior and clinical functioning, as well as to underlying gene networks and neurobiology, the study of endophenotypes offers a bridge for connecting gene-brain-behavior relationships, to help increase an understanding of the biology of a disorder, which may offer an opportunity to inform

treatment among affected individuals. This dissertation takes an endophenotype approach and deeply characterizes social attention by extrapolating dynamic looking patterns and uncovering underlying mechanistic properties including behavioral (i.e., performance-based measures and eye-tracking variables) and neural bases of bottom-up visual perception in individuals with ASD and their first-degree relatives in three separate, but theoretically related, studies.

Methods: Across tasks, participants included a maximum of 32 individuals with ASD and 30 controls, as well as 56 parents of individuals with ASD and 43 parent controls. Top-down social attention was assessed using a suite of analytical methods applied to eye tracking during presentation of a social-emotional scene, characterizing where and how participants looked. To examine bottom-up visual processing, *Global* and *Local* composite scores were generated from several eye-tracking variables obtained during two interactive tasks administered on an eye-tracker. Finally, neural correlates of local/global processing were assessed with event-related potentials (ERPs, i.e., time-locked EEG responses to visual stimuli), including P1, N1, and N2 components.

Results: The ASD and ASD parent groups showed reduced social attention over the course of the task, with a linear decrease and a dynamic looking pattern (i.e., shifting away earlier from social information and decreasing social attention later) in the ASD and ASD parent groups, respectively. Both groups also refixated more toward non-salient, background objects compared to controls, but there were no group significant differences in the transitions away from and towards social and non-social information, percentage of area explored, first fixation durations

and type of information first explored, regressive fixations, or number of fixations per second. Autistic individuals demonstrated a greater local than global visual processing style. While parent groups did not differ in Local/Global composite scores, ASD parents attended less towards global features of the stimuli than parent controls. Finally, atypical N1 amplitudes and latencies in the occipital-parietal region were found in the ASD group, with observable opposite patterns of neural responses occurring in the N2 component in both the ASD and ASD parent groups compared to controls. Social attention, and local and global gaze and neural components were related to clinical and sub-clinical features of the ASD phenotype.

Conclusions: Eye-tracking and neural results demonstrated parallel patterns of reduced social attention and global perception between individuals with ASD and, more subtly, parents of individuals with ASD, compared to controls. The eye-tracking variables examined in this study are thought to effectively reveal different aspects of underlying cognition, therefore revealing key mechanistic insights into the roots of social functioning differences in ASD. Furthermore, findings of local/global visual processing differences both behaviorally and neurally point to underlying neurobiological differences shaped by ASD-related genetic variation. Importantly, relationships with clinical and sub-clinical features of autistic individuals and parents support the utility of studying social and non-social visual perception and attention to enhance an understanding of underlying biological mechanisms contributing to ASD-related traits, potentially reflecting genetic liability to ASD. Findings further highlight the investigation of biological and mechanistic underpinnings using eye-tracking and EEG methodology to the study of visual perception/attention, which may help to elucidate the gene-brain-behavior basis of the

disorder. Finally, stimuli and methodologies applied to the present work will help to inform future studies of vision and cognitive science.

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CHAPTER 1: INTRODUCTION

Dissertation Overview

This dissertation used a multi-method, family study design to explore the neurocognitive bases of visual perception and attention in individuals with autism spectrum disorder (ASD) and their biological parents. ASD is a neurogenetic disorder characterized by social communication deficits and restricted and repetitive behaviors or interests (APA, 2013). Visual perception/attention are the crux of navigating and understanding the world. Atypicalities in bottom-up visual perception and top-down attention can lead to downstream effects in social skills, communication, and cognition more generally (Behrmann, Thomas, & Humphreys, 2006; Burnette et al., 2005; Happe, 1999; Jarrold, Butler, Cottington, & Jimenez, 2000; Jolliffe & Baron-Cohen, 2000; Klin, Jones, Schultz, Volkmar, & Cohen, 2002b), which have been documented in autistic individuals and more subtly expressed among first-degree relatives. However, it remains unknown whether such differences are linked to underlying neurobiology and whether they index genetic liability relating to a constellation of subclinical features (i.e., parallel defining qualities of ASD) documented in relatives, known as the "Broad Autism Phenotype" (BAP). Because ASD is an etiologically complex condition, studies of the BAP offer a powerful method for identifying homogenous subgroups where distinct etiologic processes might be defined and targeted in biological and treatment studies. This dissertation applied novel analyses to eye-tracking data to examine top-down visual attention (Chapter 2) and bottom-up visual perception (Chapter 1) in ASD and the BAP, as well as an examination of underlying neural correlates of visual perception using electroencephalogram (EEG) (Chapter 4). These data were also explored in relation to a broad battery of clinical-behavioral features to understand

how visual perception/attention may contribute to both clinical and sub-clinical features of the disorder. Uncovering such relationships with core features of the disorder may help to identify potential underlying biological mechanisms of the observed phenotype, contributing to the candidacy of visual perception/attention as an ASD-related endophenotype.

Eye tracking and EEG methodologies

Eye tracking can provide an indirect measurement of underlying cognitive, attentional, and executive skills, and promises meaningful information about perceptual and attentional strategies (Eckstein, Guerra-Carrillo, Singley, & Bunge, 2017). In comparison to reaction time and accuracy (i.e., performance) measures alone, eye tracking has the potential to reveal moment-to-moment information of underlying strategies and cognition (Awh, Armstrong, & Moore, 2006; Grosbras, Laird, & Paus, 2005; Just & Carpenter, 1975; Luna, Velanova, & Geier, 2008; Theeuwes, Belopolsky, & Olivers, 2009; Thomas & Lleras, 2007; Van der Stigchel, Meeter, & Theeuwes, 2006; Yarbus, 1967), revealing nuanced and dynamic patterns at an individual or group level. While there are many methods of examining eye-tracking data, the most commonly utilized metrics include the proportion of fixation counts and the length of time that a fixation occurs, as these variables are thought to reflect the time required to process the visual information and reflects attention or engagement (Eckstein et al., 2017).

Yet, these methods may lack sensitivity for capturing more nuanced patterns of eye movement reflective of everyday attentional dynamics. Capturing visual attentional patterns granularly using unique metrics and temporal dynamics allows a vivid illustration of the attentional trajectories that unfold over time, reflecting the dynamic (versus static) process of

attention in the real world. For example, perseverations (repeat successive fixations towards the same area) may reflect "sticky attention" or mental disengagement (Hughes & Russell, 1993), or regressions (i.e., refixating on previously examined areas) indexes the loss of mental set or executive control, as well as an indication of information that may repeatedly capture an individuals' attention (R. W. Booth & Weger, 2013; Perea & Carreiras, 2003; Rayner, 1998; Rayner, Slattery, & Belanger, 2010), or examining fixations over the course of a stimulus, which reflects dynamic patterns of looking more characteristic to daily life. As such, while traditional methods of dwell time and fixations can reveal important information on information processing, it may obscure the discovery of nuanced patterns of thinking or cognition. It is therefore essential to examine various patterns of looking behavior during eye-tracking paradigms allowing a more sensitive and thorough investigation of underlying cognition thought to be impacted in ASD.

Electroencephalogram (i.e., EEG) provides an opportunity to study the underlying neural mechanisms that dictate information processing and behavior more directly than eye tracking. Electrical impulses between neurons and different areas of the brain are exchanged, reflecting communication through coordination and integrative processes. EEG can measure these electrical signals (both the size and the timing) that are triggered in response to different types of input (e.g., visual or auditory stimuli), which are also known as event related potentials (or, ERPs). ERPs can therefore directly offer the underlying neural correlates related to observed sensory or cognitive processes, including behavior documented via eye tracking. As such, ERPs can operate as measurable endophenotypes along the pathway of phenotype and genotype, thereby representing simpler clues to underlying genetic mechanisms than behavior alone (Kropotov, Mueller, & Ponomarev, 2011). For example, early sensory components in response to

auditory stimuli have been found to be diminished in patients with bipolar disorder with psychosis, with similar attenuation observed in their first-degree relatives (Schulze et al., 2007), suggesting that P50 responses may be an endophenotype for the disorder. Identification of endophenotypes therefore confers a powerful tool for early identification and diagnosis of a disorder such as ASD, which is critical for early intervention that often results in more positive outcomes (e.g., see review R. J. Landa, 2018). Additionally, the usage of EEG methods can help to identify cognitive and biological features that may mechanistically contribute to the clinical-behavioral phenotypes in autism, bringing us close to disentangling the heterogeneous and complex ASD phenotype.

Studies of gaze and ERP in ASD have revealed unique patterns of visual processing indirectly and directly (Baruth, Casanova, Sears, & Sokhadze, 2010; Chita-Tegmark, 2016; Dalton et al., 2005; Dawson et al., 2005; Frazier et al., 2017; Jeste & Nelson, 2009; J. C. McPartland, Webb, Keehn, & Dawson, 2011; Stroganova, Orekhova, et al., 2007; Stroganova et al., 2012; Van der Hallen, Evers, Brewaeys, Van den Noortgate, & Wagemans, 2015; Van Eylen, Boets, Steyaert, Wagemans, & Noens, 2018). Such patterns have also been shown to relate to clinical features in ASD (Behrmann et al., 2006; Burnette et al., 2005; Fitch, Fein, & Eigsti, 2015; Happe, 1999; Jarrold et al., 2000; Jolliffe & Baron-Cohen, 2000; Klin et al., 2002b; Van Eylen et al., 2018), and are present in more subtle forms among first-degree relatives of individuals with ASD (Adolphs, Spezio, Parlier, & Piven, 2008; Bolte & Poustka, 2006; M. Lee et al., 2019; Losh et al., 2009; Mosconi et al., 2010; Nayar et al., 2018; Yucel et al., 2015). Studies of visual perception/attention are therefore promising avenues to identify ASD-related endophenotypes. Finally, because the clinical presentations and etiology of ASD are

heterogeneous, this dissertation importantly contributes to efforts characterizing the biological basis of the disorder. Identifying brain-behavior pathways via the application of multimodal assessments whereby both complex phenotypes (e.g., clinical and sub-clinical phenotypes involving social communication) and their fundamental contributing processes (e.g., visual perception, social attention, neural underpinnings) are investigated in tandem, may help in the development and evaluation of interventions. Specifically, biological mechanisms identified in this dissertation may be targeted in clinical interventions and used to measure heterogeneous response to intervention common to ASD, particularly through the identification of subgroups or co-occurring mechanistic pathways.

Family-study designs

This dissertation used eye tracking and EEG to detail the specific visual perceptual and attentional profiles in families of individuals with ASD and their relationship with underlying clinical-behavioral phenotypes as a means to uncover biological underpinnings of ASD-related features. Assessing these characteristics in parent-child dyads can help to identify ASD endophenotypes that may help to unpack the heterogeneity of ASD. Because the genetics underlying ASD are very complex (i.e., the majority of cases of ASD are polygenic in nature, with many contributing genes) (Bulik-Sullivan, Finucane, et al., 2015; Bulik-Sullivan, Loh, et al., 2015; De Rubeis et al., 2014; Gauglerl et al., 2014; Iossifov et al., 2014; Sanders et al., 2015), research aimed at characterizing the heterogeneity of ASD may lead to evidence-based approaches to inform prevention or treatment.

A precise understanding of the full range and nature of ASD-associated phenotypes is necessary to maximize our ability to elucidate the biological basis of this condition. The full range of the ASD phenotype may be characterized according to both clinical and subclinical features. Specifically, the broad autism phenotype (BAP) are milder characteristics that are associated with ASD but are not associated with functional impairment, and have been observed to segregate independently in unaffected relatives (i.e., social aloof features or rigid tendencies versus both) (Constantino & Todd, 2003; Losh, Adolphs, & Piven, 2011; Losh, Childress, Lam, & Piven, 2008; Piven, Palmer, Jacobi, Childress, & Arndt, 1997), therefore offering the study of isolated traits that is by definition not possible in ASD, and potentially reflecting distinct genetic contributions to the characteristic ASD symptoms (Davidson et al., 2014; Gottesman & Gould, 2003; Happe, Ronald, & Plomin, 2006; Losh et al., 2011). Additionally, first-degree relatives of individuals with ASD likely have fewer comorbidities than the clinical disorder (and therefore reduced polygenic influence), thus providing a more refined phenotypic expression of genetic liability to ASD. Studying the BAP and subclinical traits related to ASD therefore provides a potentially more straightforward pathway to the underlying genetic etiology of said traits relative to the complex and heterogeneous symptom expression in ASD (Woodbury-Smith et al., 2018). As such, this dissertation provides a critical step in deeply phenotyping the complex ASD profile through the study of biological and cognitive underpinnings, thus helping to address the biological basis of the disorder. This dissertation is the first study to apply in a single sample of individuals with ASD and their biological parents, detailed and unique methods of characterizing visual perception and attention in both social and non-social tasks and their underlying neural

correlates to address cognitive and biological mechanisms contributing to the full range of the ASD phenotype.

Visual perception in ASD

An essential component of visual perception is global processing, which is rapid and automatic (Colombo, Mitchell, Coldren, & Freeseman, 1991; Freeseman, Colombo, & Coldren, 1993; Poirel, Pineau, & Mellet, 2008) and involves the integration of local elements of a scene to create a whole (Kimchi, 1992; Navon, 1983). This process exhibits an extended developmental trajectory from local to global processing with age (Nayar, Franchak, Adolph, & Kiorpes, 2015) and is usually the default perceptual strategy used by adults (Navon, 1977b). In contrast, local perception is the selective attention to parts of a scene (Kovacs, 1996; Navon, 1983), and is usually the characteristic perceptual style of young children, and also generally slower than global processing (Freeseman et al., 1993; Kimchi, 1992; Navon, 1977b; Nayar et al., 2015). These processes in tandem support the fluid interpretation of our environment and social worlds in particular, as impairments in seeing the "big picture" can lead to downstream effects in social skills, communication, and cognition more generally (Behrmann et al., 2006; Burnette et al., 2005; Happe, 1999; Jarrold et al., 2000; Jolliffe & Baron-Cohen, 2000; Klin et al., 2002b).

The central coherence theory of autism (Happe & Frith, 2006) posits that features of ASD arise in part from a tendency to favor local versus global stimuli, and reduced integration into context. Differences in visual perceptual styles, including a local perceptual bias with or without deficits in global processing (e.g., Van der Hallen et al., 2015) are thought to underscore aspects of the social communication difficulties observed in ASD, such as fixating on one part of the

face, making it challenging to interpret facial expressions (Behrmann et al., 2006; Burnette et al., 2005; Happe, 1999; Jarrold et al., 2000; Jolliffe & Baron-Cohen, 2000). Specifically, weak central coherence, including a local perceptual bias at the expense of global processing, along with a tendency to visually perseverate have been hypothesized to underlie key features of ASD (e.g., Happe & Frith, 2006; Klin et al., 2002b; Sasson, Turner-Brown, Holtzclaw, Lam, & Bodfish, 2008), such as aspects of learning, social functioning, and RRBs (Koegel & Covert, 1972; Sasson, Dichter, & Bodfish, 2012; Sasson et al., 2008; Varni, Lovaas, Koegel, & Everett, 1979). Taken together, local perceptual styles may be a mechanistic contributor to the social attentional differences observed in ASD, and subsequently the social-communicative challenges inherent to the disorder. Therefore, studies of visual perception and social attention allow for an in-depth investigation into the underpinnings of a key aspect of ASD.

Visual perception and attention in the BAP

Family members of individuals with ASD may demonstrate a constellation of subclinical features believed to index genetic liability to ASD (i.e., the broad autism phenotype, BAP) (Bailey, Palferman, Heavey, & Le Couteur, 1998; Bailey & Parr, 2003; Le Couteur et al., 1996; Losh et al., 2009; Losh et al., 2008; Losh & Piven, 2007; Pickles et al., 2000). Differences in visual perception have been observed in ASD family members when assessing global form processing, social cognition, gaze-language coordination, and language use (Adolphs et al., 2008; Bolte & Poustka, 2006; Briskman, Happe, & Frith, 2001; Chouinard, Unwin, Landry, & Sperandio, 2016; Constantino et al., 2017; Cribb, Olaithe, Di Lorenzo, Dunlop, & Maybery, 2016; Hogan-Brown, Hoedemaker, Gordon, & Losh, 2014; M. Lee et al., 2019; Mosconi et al.,

2010; Nayar et al., 2018). Evidence suggests that relatives of individuals with ASD may demonstrate a preference for local features of a visual scene compared to controls (Bolte & Poustka, 2006; Briskman et al., 2001; Van Eylen et al., 2017). A recent study demonstrated reduced susceptibility to non-social illusions as a function of traits related to the BAP (Chouinard et al., 2016). Additionally, parents of individuals with ASD were shown to pay greater attention to details in daily life on a self-report questionnaire (Roberts, Barthel, Lopez, Tchanturia, & Treasure, 2011), with inconsistent findings using neuropsychogical assessments (Van Eylen et al., 2017). It is possible that more objective and sensitive assessments may better capture subtle differences evident in elements of the visual perceptual styles in the BAP. For example, Adolphs and colleagues (2008) showed that parents with the BAP devoted less attention to the eyes during a facial processing task, which was associated with specific neural correlates showing increased amygdala and fusiform gyrus activation to faces compared to control parents (Yucel et al., 2015), displaying striking similarities to patterns observed in ASD. Additionally, evidence has demonstrated less fluent eye movement patterns during a visually-based language processing task in both individuals with ASD and siblings (Hogan-Brown et al., 2014), with similar patterns emerging in parents of individuals with ASD (M. Lee et al., 2019; Nayar et al., 2018), reflecting a reliance on different *perceptual* styles versus a breakdown in motor control for instance. These studies highlight the importance of using objective and sensitive measures such as eye tracking (as opposed to performance-based measures of accuracy and reaction time alone) to capture often subtle, yet significant differences in ASD and the BAP. Because eye tracking affords a window into underlying cognition, directly studying brain responses is a critical next step in elucidating the biological bases of an important aspect of the ASD phenotype. Yet, the

underlying neural response patterns associated with visual perception remain relatively unexplored in ASD and, to our knowledge, this dissertation was the first study to explore neurocognitive underpinnings of local-global perception in non-social stimuli in ASD *and* their parents.

Neural underpinnings of visual processing in ASD and the BAP

Many studies have examined the neural underpinnings of local and global perception in the typical and atypically developing populations. Typically, perceivers using a global strategy tend to recruit higher order visual areas of the brain (Harris, Schwarzkopf, Song, Bahrami, & Rees, 2011; Ringach & Shapley, 1996; Stanley & Rubin, 2003), relative to when using a local strategy, during which lower, early visual areas are involved (T. S. Lee & Nguyen, 2001; Maertens & Pollmann, 2005). EEG/ERP studies have also been used to assess local and global perception in neurotypical development (e.g., T. S. Altschuler et al., 2014; Altschuler et al., 2012; Brown, Gruber, Boucher, Rippon, & Brock, 2005; Kruggel, Herrmann, Wiggins, & von Cramon, 2001; M. M. Murray, Foxe, Javitt, & Foxe, 2004; Stroganova, Orekhova, et al., 2007; Stroganova et al., 2012; Sugawara & Morotomi, 1991; Tallon-Baudry, Bertrand, Wienbruch, Ross, & Pantev, 1997).

Converging evidence in the typical population has revealed a signature ERP response occurring during global perception (E. L. Altschuler et al., 2014; Altschuler et al., 2012; Ffytche & Zeki, 1996; Hirsch et al., 1995; M. M. Murray, Imber, Javitt, & Foxe, 2006; M. M. Murray et al., 2002; Proverbio & Zani, 2002; Ritzl et al., 2003), characterized by a higher amplitude of the N1 component (first negative deflection) and a later N_{cl} response (Foxe, Murray, & Javitt, 2005;

C. S. Herrmann & Bosch, 2001; Proverbio & Zani, 2002; van Dinteren, Arns, Jongsma, & Kessels, 2014). In contrast, there is an immature N1 component in young neurotypical children (<6 years) (T. S. Altschuler et al., 2014) and in children with ASD (Stroganova, Orekhova, et al., 2007). Results of different neural patterns in response to KICs are consistent with previous work demonstrating less automatic global processing abilities in neurotypical young children (Nayar et al., 2015) and ASD (Nayar, Voyles, Kiorpes, & Di Martino, 2017). As such, there is emerging evidence for the biological underpinnings of the local/global visual processing differences observed in ASD, and potentially a marker of the core social-communicative features of the disorder.

Importantly, neural markers indexing early sensory processing in extrastriate visual areas (e.g., P1 and P3 components) are often also involved in global perception and attentional processes more generally (Foxe, Doniger, & Javitt, 2001; Foxe et al., 2005; C. S. Herrmann & Mecklinger, 2001; C. S. Herrmann, Mecklinger, & Pfeifer, 1999; C. S. Herrmann, Munk, & Engel, 2004; van Dinteren et al., 2014). P1 is impaired in atypical development (Foxe et al., 2001; Foxe et al., 2005) and P3 shows a protracted developmental trajectory (van Dinteren et al., 2014). P1 and P3 therefore become important to study in ASD, given documented sensory processing/attentional atypicalities (Chita-Tegmark, 2016; Frazier et al., 2017; Marco, Hinkley, Hill, & Nagarajan, 2011; Papagiannopoulou, Chitty, Hermens, Hickie, & Lagopoulos, 2014; Robertson & Baron-Cohen, 2017), also observed more subtly in the BAP (Adolphs et al., 2008; Bolte & Poustka, 2006; Briskman et al., 2001; Chouinard et al., 2016; Constantino et al., 2017; Cribb et al., 2016; Hogan-Brown et al., 2014; M. Lee et al., 2019; Mosconi et al., 2010; Nayar et al., 2018).

Together, atypical local/global perception has been demonstrated at the behavioral, neuropsychological, and neural levels in young neurotypical children and to some extent in children with ASD, though additional studies are needed to inform the inconsistent findings in the literature (likely due to methodological differences and the inherent heterogeneity in ASD). Further, it remains unknown whether the emerging neural differences in local/global perception relate to clinical-behavioral features of ASD, which is critical to understanding the mechanistic contributions specific to the ASD phenotype. Importantly, no study has investigated these mechanisms in older children with ASD, when adult-like global perception has developed in the neurotypical population, which is important to further delineate typical developmental processes from atypical development. Finally, although studies have generally found EEG/ERP differences among siblings of individuals with ASD (Levin, Varcin, O'Leary, Tager-Flusberg, & Nelson, 2017; Tierney, Gabard-Durnam, Vogel-Farley, Tager-Flusberg, & Nelson, 2012), suggesting that differences may be reflected in the BAP among parents as well, to our knowledge, no study has examined mechanistic processes of visual perception/attention in parents. This revealed a critical gap in the search for endophenotypes and biological underpinnings of ASD that was directly addressed in this dissertation.

Summary

This dissertation represents a natural extension of prior work as it incorporated a range of theoretical, methodological, and analytic tools to studying brain-behavior characteristics related to ASD through three complementary studies. First, we examined top-down visual social attention using a suite of eye-tracking analytical tools applied to eye-tracking data obtained from

individuals with ASD and parents. Second, we examined bottom-up visual perception (specifically, local and global visual processing) as a means to understanding the social attentional differences in autistic individuals and their parents. Finally, we unpacked the underlying neural mechanisms of early visual processing using EEG/ERP methodologies in both individuals with ASD and parents. Together, this dissertation examined local and global processing by applying eye-tracking and EEG methodologies in order to better understand the neurocognitive mechanisms that underlie the well-documented visual perceptual differences in ASD, with the addition of exploring the same in first-degree relatives.

Results from this dissertation have the potential to contribute to an understanding of key cognitive and neural systems affected by ASD genetic risk, with implications for better understanding the biology of ASD that may lead to earlier diagnosis as well as objective measures that may be used to monitor treatment progression. Finally, results from this dissertation may help to inform cognitive theories related to ASD, particularly those pertaining to the weak central coherence (i.e., impairments in global processing) (Happe & Frith, 2006) and enhanced perceptual functioning (i.e., a bias towards local processing with or without global processing impairments) (Bertone, Mottron, Jelenic, & Faubert, 2005; F. G. Happe, 1996; Jolliffe & Baron-Cohen, 1997; Joseph, Keehn, Connolly, Wolfe, & Horowitz, 2009; Kemner, van Ewijk, van Engeland, & Hooge, 2008; Minshew, Goldstein, & Siegel, 1997; O'Riordan & Plaisted, 2001; Shah & Frith, 1983, 1993) theories, in addition to cognitive profiles and underlying neural circuitry contributing to the disorder. It may additionally help to specify potential underlying causes of aspects of the BAP, helping to not only further define it but also to elucidate differences between causes for ASD phenotypic characteristics versus milder sub-

clinical features. The potential for identifying subgroups with social attentional and visual perceptual deficits may further contribute to unpacking the inherent heterogeneity in ASD, thus delivering fruitful mechanisms of action contributing to heterogeneous responses to intervention often seen in ASD. Taken together, identification of biomarkers related to ASD in affected and unaffected individuals, such as those potentially identified through this dissertation, may aid in stratifying individuals into biologically and clinically meaningful subgroups with certain biomarker profiles, that would allow for a more homogenous sample for future genetic and treatment studies.

CHAPTER 2: A comprehensive examination of eye-tracking analytical tools and their application in ASD and the broad autism phenotype

Abstract

Background**:** Traditional eye-tracking methods involve taking the percentage of the total fixation count or fixation duration occurring towards specific a priori areas of interest (AOI). However, such methods may obscure gaze patterns that reflect the dynamic nature of visual attentional mechanisms that are characteristic of gaze in daily life. This study examined the utility of applying a suite of eye-tracking analyses that extends beyond traditional analytical methods of gaze to an autism family-study framework. Differences in social attention have been well documented in individuals with autism spectrum disorder (ASD), a neurogenetic disorder characterized by social impairments and the presence of restricted and repetitive behaviors. Recent work has revealed subtle differences in social attention in parents of individuals with ASD relative to parent controls, suggesting the possibility for a shared genetic link to visual attention that is further influenced by ASD-risk genes. An application of nuanced analytic methods on eye-tracking data in these populations may help to uncover subtle differences and commonalities observed among unaffected individuals, which may be missed by traditional analytic approaches.

Methods: Participants included 37 individuals with ASD, 38 controls, 151 parents of individuals with ASD, and 63 parent controls. A complex scene from the thematic apperception test depicting a woman in the foreground, with several social and non-social information in the background and periphery of the stimuli, was displayed on an eye tracker. Participants were tasked to narrate a story following the image, which was displayed for 8 seconds. AOIs included

social versus non-social information and analytical methods included the following themes of variables: 1) Traditional overall gaze variables, 2) Dwell time patterns (e.g., analyzing gaze over the course of the task), 3) Fixation patterns (e.g., perseverative or regressive fixations), and 4) Distribution patterns regardless of AOI. A series of MANOVAs, growth curve analyses, or Chi-squared analyses were applied to examine group differences separately for ASD versus control groups and ASD parent versus parent control groups.

Results: While no differences between groups emerged in distribution pattern variables for ASD and ASD parent groups relative to respective control groups, several differences emerged when applying unique analytical methods to gaze data. In particular, individuals with ASD and their parents evidenced reduced social attention over the course of the stimulus presentation, with differences emerging half way into the stimulus presentation for the ASD group and the second half of the stimulus presentation for the ASD parent group. Additionally, decreased social and increased non-social perseverative fixations was observed among ASD and ASD parent groups relative to controls. Findings in the ASD parent group were particularly driven by a subset of parents with features of the broad autism phenotype (BAP), which are a constellation of personality and language features mirroring the core symptoms of ASD and indicate increased genetic liability to the disorder.

Conclusions: Analytical methods examining fixations over the course of the task and perseverative fixations were most robust in differentiating ASD and the BAP parent groups from controls. This study therefore highlights the utility of applying growth curve and time-bin

analytic methods to examine fixations over time in studies of eye-tracking more generally and in studies of visual attention (social or non-social) in ASD and the BAP more specifically. Although other analytical methods applied to this project showed few differences between groups, they remain a valuable set of methodological tools as they too capture dynamic looking patterns that are thought to reflect different aspects of underlying cognition, namely, social attention. In sum, this study presents 11 objective and measurable eye-tracking variables, and thus serves as a proof-of-concept for future eye-tracking studies examining visual attention across any population. It further highlights the utility of applying complex analytic methods to studying visual attention in ASD and the BAP, particularly to capture subtle patterns of underlying social-emotional differences in these groups.

Introduction

Eye tracking can provide an indirect measurement of underlying cognitive, attentional, and executive skills, and promises meaningful information about perceptual and attentional strategies (Eckstein et al., 2017). The earliest of eye-tracking studies (Yarbus, 1967), and several others following (Just & Carpenter, 1975; Theeuwes et al., 2009; Thomas & Lleras, 2007; Van der Stigchel et al., 2006), have demonstrated that the location of gaze (i.e., where individuals look when exploring stimuli) not only reflects attentional processes (Awh et al., 2006; Grosbras et al., 2005), but also maps onto underlying thoughts and cognition (Eckstein et al., 2017). Early studies have argued the utility of eye-tracking methods as being complementary and associated to both behavioral (e.g., accuracy and reaction time indices) and neural measurements of cognition (Luna et al., 2008). In comparison to reaction time and accuracy performance measures, eye-tracking has the potential to reveal moment-to-moment information of underlying cognition, revealing nuanced and dynamic patterns at an individual or group level. Eye-tracking technology, while reflecting an indirect measurement of underlying brain function, has several advantages over brain imaging technologies, as outlined in (Eckstein et al., 2017). Additionally, dependent on the type of stimuli, analyses of gaze could index activity in areas of the brain associated with visual processing (e.g., social stimuli and amygdala activation) (Dalton et al., 2005; Sabatinelli et al., 2011; Yucel et al., 2015).

As such, analysis of gaze may provide an intermediate link between biology and behavior, with the potential of revealing cognitive differences that may stem from underlying neurobiology. The use of eye tracking has been fruitful as a means to explore social cognitive atypicalities in autism spectrum disorder (ASD) (Klin, Jones, Schultz, Volkmar, & Cohen,

2002a; Klin et al., 2002b; Pelphrey et al., 2002). Differences in visual attention have been repeatedly documented in individuals ASD (Chita-Tegmark, 2016; Frazier et al., 2017; Papagiannopoulou, Chitty, Hermens, Hickie, & Lagopoulos, 2014), which have been shown to relate to social communication impairments (Klin et al., 2002b; M. Lee et al., 2019; Navab, Gillespie-Lynch, Johnson, Sigman, & Hutman, 2012; Righi et al., 2018; Speer, Cook, McMahon, & Clark, 2007) and restricted and repetitive behaviors (Nayar et al., 2018; Sasson et al., 2008), core features of the disorder. Gaze and eye movement differences can be detected as early as infancy in individuals with ASD. For instance, whereas infant controls show difficulty disengaging visual attention from faces, infants with ASD show comparable disengagement from faces and objects (Chawarska, Volkmar, & Klin, 2010), revealing a lack of preference towards faces. Additionally, infants with ASD also scan key face areas atypically (Chawarska & Shic, 2009; Falck-Ytter, Fernell, Gillberg, & von Hofsten, 2010; Jones, Carr, & Klin, 2008; Nakano et al., 2010) and show reduced preference for biological motion (Klin, Lin, Gorrindo, Ramsay, & Jones, 2009) as well as social elements of a scene (Klin & Jones, 2008; Shic, Bradshaw, Klin, Scassellati, & Chawarska, 2011). These atypicalities persist into adolescence and adulthood, wherein individuals with ASD continue to explore scenes depicting social and non-social elements differently compared to typically developing controls, demonstrating slower latencies to orient to social features of the scene (Sasson et al., 2008; Unruh et al., 2016) and different scanning patterns (Frazier et al., 2017; Wang, Campbell, Macari, Chawarska, & Shic, 2018); though findings vary depending on the type of stimulus (Chevallier et al., 2015; Speer et al., 2007). For example, when there is competing information in the scene (i.e., both salient and non-salient features), individuals with ASD tend to explore non-salient aspects of the scene (e.g.,

objects or non-eye regions of the face) more than controls (Chawarska, Macari, & Shic, 2012; Frazier et al., 2017; M. Lee et al., 2019; Shic, Chawarska, Bradshaw, & Scassellati, 2008), which has been shown to relate to reduced social competency (Falck-Ytter et al., 2010; Klin et al., 2002b).

Evidence also suggests that eye movement patterns are heritable in the general population (Constantino et al., 2017) and across psychiatric disorders (Ettinger et al., 2004), suggesting that eye movements and visual attention may not only reflect underlying genetics (i.e., constituting endophenotypes, which are heritable characteristics associated with the genetic underpinnings of a disorder (Gottesman & Gould, 2003)), but also neurobiological mechanisms contributing to the development of a disorder's symptomatology. As such, family studies of gaze in individuals with ASD and their relatives has the potential to inform the mechanistic processes related to the etiology and development of ASD symptomatology. Evidence exists that first-degree relatives of individuals with ASD may also demonstrate subtle differences in visual attention (Adolphs et al., 2008; Constantino et al., 2017; M. Lee et al., 2019; Pierce et al., 2016), which have been linked to features related to the broad autism phenotype (BAP; a constellation of subclinical traits that mirror the core symptoms of ASD, thought to reflect genetic liability to ASD) such as aloofness (Adolphs et al., 2008; Losh et al., 2008; Losh & Piven, 2007), suggesting that visual attention may be a marker of genetic risk to ASD that is also related to broader ASD features.

Ongoing studies have aimed to understand the utility of looking patterns as endophenotypes or biomarkers in ASD (Bradshaw et al., 2019; Murias et al., 2018; Pierce et al., 2016). For example, Adolphs and colleagues (2008) showed that parents with the BAP devoted less attention to the eyes during a facial processing task using the "bubbles" method (i.e.,

blurring portions of the face), displaying striking similarities to patterns observed in ASD. This pattern of face processing in parents of individuals with ASD has been associated with specific neural correlates, showing increased amygdala and fusiform gyrus activation to faces compared to control parents (Yucel et al., 2015). Groen and colleagues (2012) have also reported reduced visual attention to social aspects of the scene in both individuals with ASD and their parents. Studying family members who are at increased genetic risk to ASD has also revealed differences in language competence, social cognition, and eye-voice coordination among parents and siblings of individuals with ASD, particularly among those displaying the BAP (Hogan-Brown et al., 2014; M. Lee et al., 2019; Losh et al., 2009; Losh, Esserman, & Piven, 2010; Losh & Piven, 2007; Nayar et al., 2018). Recent work (M. Lee et al., 2019) has demonstrated gaze differences emerging among individuals with ASD and their parents with the BAP compared to respective control groups during a complex social scene, which contrasted with a lack of gaze differences emerging during a more structured picture-book task. In particular, findings showed that individuals with ASD and the BAP (compared to controls) attended more towards the non-social setting elements of a key image depicting a detailed background and a foreground image of a woman with an ambiguous facial expression. Together, this work demonstrates the utility of studying looking patterns as potentially good candidate endophenotypes given their known heritability and association with ASD. However, visual attention and related eye movement patterns have been examined using primarily global fixation measures across many different stimuli across studies, and have been understudied in first-degree relatives, particularly in parents of individuals with ASD with the BAP (to the author's knowledge, only three studies to date

have examined visual perception/attention using eye tracking in parents) (Groen et al., 2012; M. Lee et al., 2019; Nayar et al., 2018).

It remains unknown, however, how differences in gaze in prior work studying visual attention in ASD and the BAP might change over the course of a stimulus presentation, and whether groups demonstrate widespread visual scanning across numerous areas of interest, or whether they show a pattern of reduced scanning, seemingly showing attentional "stickiness" (Chita-Tegmark, 2016; Nayar et al., 2018; Papagiannopoulou et al., 2014; Sasson et al., 2008; F. Shic, K. Chawarska, & B. Scassellati, 2008a). The most commonly utilized metrics in research using eye tracking include the proportion of the total number of fixations and the length of time that a fixation occurred (i.e., dwell time), as these variables are thought to reflect attention allocation, attentional engagement, and the time required to process visual information (Eckstein et al., 2017). There are, however, many different methods to examining eye-tracking data, which may reveal different aspects of cognition. For example, perseverations (repeat successive fixations towards the same area) may reflect "sticky attention" or mental disengagement (Hughes & Russell, 1993), or regressions (i.e., refixating on previously examined areas) indexes the loss of mental set or executive control, as well as an indication of information that may repeatedly capture an individuals' attention (R. W. Booth & Weger, 2013; Perea & Carreiras, 2003; Rayner, 1998; Rayner et al., 2010), or examining fixations over time, which reflects dynamic patterns of looking more characteristic to daily life. As such, while traditional methods of dwell time and fixations can reveal important information on information processing, it may obscure the discovery of nuanced patterns of thinking or cognition. It may therefore be even more meaningful to examine various patterns of looking behavior during eye-tracking paradigms. As

such, focused analysis involving moment-to-moment gaze patterns may reveal more nuanced fixation trajectories that have been found in recent work of gaze and ASD (Constantino et al., 2017), that may not otherwise be captured via global indices of fixation counts and duration.

Evidence suggests that results dependent on typical fixation measures are heavily influenced by processing methods (F. Shic, K. Chawarska, & B. Scassellati, 2008b; Wass, Forssman, & Leppänen, 2014; Wass, Smith, & Johnson, 2013), and have been shown to dramatically alter findings in ASD (Shic, Chawarska, et al., 2008b). Additionally, they provide only a general overview of looking patterns. Ongoing studies have demonstrated the efficacy of exploring perseverative (repeated fixations within the same area of interest; AOIs) and regressive (repeated fixations towards previously-explored AOIs) fixations in ASD and the BAP in social and non-social stimuli, and which were found to relate to ASD symptomatology (Nayar et al., 2018; Sasson et al., 2008). Shic and colleagues utilized Transition Entropy Analyses in young children with ASD (Shic, Chawarska, Bradshaw, et al., 2008), finding no changes in the transitions of fixations (i.e., transitions from one AOI to another) between salient and non-salient regions of the face in individuals with ASD, unlike controls, thus demonstrating differences in patterns of attention allocation between groups. The authors also implemented Spatial Distribution Analysis or Nearest Neighbor Index (i.e., distance-dispersion algorithm) in children with and without ASD, to explore how fixations were dispersed across the facial stimuli (Shic, Chawarska, et al., 2008a). Importantly, this method was resistant to changes in fixation parameter algorithms (in comparison to mean fixation duration or dwell time) (Shic, Chawarska, et al., 2008b; Wass et al., 2014; Wass et al., 2013), highlighting the efficacy of utilizing such a method in analyzing gaze differences in this population. Finally, growth curve analyses (GCA),

proves to be a rigorous method of assessing changes over the course of time, which can be applied to understand the moment-to-moment pattern of gaze while interpreting a scene. In particular, GCA maps out the time-linked gaze trajectory over the course of the stimulus presentation and can elucidate changes occurring longitudinally across developmental time periods. Though not identical to GCA, Jones and Klin (2013) utilized latent growth curves to demonstrate that attention to the eyes are typical in infants with ASD up to 2 months of age, followed by a decline from 2-6 months of age, highlighting the efficacy of applying trajectory models of analyses to eye-tracking data.

These studies highlight the utility of analyzing eye-tracking data using multiple analytic methods to investigate gaze differences in ASD and the BAP. As such, the aim of this study was two-fold: 1) to provide a suit of eye tracking analytic tools that can be applied to eye-tracking studies of visual attention in typical and atypical development, and 2) to apply these methods to ASD and the BAP with the goal of identifying potentially subtle top-down social visual attentional differences in these groups compared to controls, which may be obscured by global analyses of looking time or fixations, and be more sensitive in capturing subtle differences present in non-clinical populations such as the BAP. Given that the purpose of this paper was methodological in nature in addition to its application to ASD and the BAP, analyses were considered exploratory and primarily to serve as a proof-of-concept. Nonetheless, based on prior the aforementioned studies, it was predicted that individuals with ASD and their parents (particularly those with features of the BAP) would show reduced social attention and increased attention to non-salient components of the scene, reflective of atypical social attention. A larger number of refixations (repeated fixations) was also expected, with decreased spatial distribution

of fixations, a greater percentage of non-social first fixations, and atypical transition entropy and looking patterns over the course of the task compared to controls.

Methods

Participants (Table 2.1)

Participants included in the present study were identical to those included in a prior study exploring language and related looking patterns (M. Lee et al., 2019). Twenty-nine individuals with ASD (ASD group) and 34 control participants (control group), as well as 74 parents of individuals with ASD (ASD parent group) and 45 control parents (control parent group) were included in the study. Inclusion criteria for individuals with ASD and controls included being 15 years of age and older and having a Full Scale IQ (FSIQ) and Verbal IQ (VIQ) ≥ 80. Participants were excluded for any severe psychiatric disorder (e.g., schizophrenia, bipolar disorder) and uncorrected vision impairments (e.g., strabismus). Participant characteristics are outlined in *Table 2.1*. All procedures were approved by the University's Institutional Review Board and written informed consent/assent were obtained for all participants.

Individuals with ASD were included following confirmation of ASD with gold standard instruments (Autism Diagnostic Observation Schedule-General or 2nd Edition (ADOS) (Lord et al., 2012) and/or the Autism Diagnostic Interview-Revised (ADI-R) (Lord, Rutter, & Le Couteur, 1994). Parents of an individual with ASD were included if they had at least one child with idiopathic ASD, and control participants were required to have no personal or family history of ASD or related genetic disorders (e.g., fragile X syndrome). BAP status was assessed in the ASD parent group only, given low base rates of the BAP among individuals without a family history of ASD (Losh et al., 2008; Piven, Palmer, Landa, et al., 1997; Sasson et al., 2013).

BAP status was assessed using the Modified Personality Assessment Scale-Revised (MPAS-R) (Piven, Palmer, Landa, et al., 1997), which includes a series of questions specifically designed to tap the subclinical features related to the BAP including aloof, rigid, perfectionistic, and untactful personality traits. Coding of personality features followed methods outlined in prior work, such that raters were assigned scores ranging from 0 to 2 (trait absent, possibly present, definitely present) on a 5-point Likert scale.

Eye tracking procedures

General procedures

Participants were asked to narrate a story after looking at an image being presented for 8 seconds on a 17-inch TFT LCD (1,280 x 1,024 resolution) Tobii T60 series eye tracker (Tobii Technology AB, Danderyd, Sweden). All participants were seated 50-60 cm from the screen and had their gaze calibrated prior to task administration, including using a standard 5-point calibration grid, which has a visual angle accuracy of 0.5°. Participants were recalibrated following any large movements. Tracking was monitored live during task administration using Tobii Studio's built-in live view and track window options, with additional calibration checks embedded in the task (e.g., center crosshair, corner star) to ensure tracking accuracy.

Eye tracking task

The Thematic Apperception Test (TAT) (H. A. Murray, 1943) was developed as a psychological projective test, and has been used in numerous studies of narrative elicitation (Beaumont & Newcombe, 2006; Hiraishi et al., 2012; M. Lee et al., 2018; M. Lee et al., 2019;

Turk, Brown, Symington, & Paul, 2010). Prior work (M. Lee et al., 2019) has demonstrated gaze differences in ASD and ASD parent groups when generating stories from TAT stimuli. The current study focused on the "Farmland Scene" (greyscale card 2; *Fig. 2.1A*) from the TAT, because of its complexity and prior findings that global indices of fixation revealed differences in attention to setting and protagonists among individuals with ASD and their parents with the BAP (M. Lee et al., 2019).

A

B

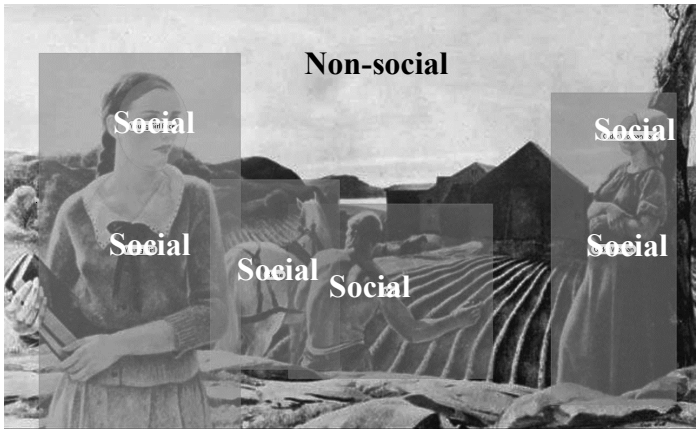

Figure 2.1. *A) TAT image examined—Card 2; Farmland Scene; B) Two primary areas of interest (AOIs) were generated—Social AOI, which included all the characters in the image; and Non-social AOI, which included everything else such as the book, barn, field.*

***Table 2.1*:** Sample Characteristics

	Control Group			ASD Group			Group Difference		
	M	**Range**	**SD**	**M**	**Range**	**SD**	***t***	**df**	***p***
Probands n (M/F)		**32 (15/17)**			**24 (18/6)**		-	-	-
Age (years)	20.90	15 - 33.25	5.15	23.82	15.19 - 57.46	9.28	-1.50	54	0.139
FSIQ	116.0	89 - 135	12.1	110.3	83 - 131	12.9	1.70	54	0.095
VIQ	118.1	93 - 138	11.9	108.8	84 - 132	13.1	2.80	54	**0.007**
PIQ	110.8	79 - 129	13.1	110.1	68 - 131	15.1	0.19	54	0.847
ADOS Total Severity Score^	-	-	-	6.1	1 - 9	2.3	-	-	-
SA Severity Score	-	-	-	5.8	2 - 9	1.9	-	-	-
RRB Severity Score	-	-	-	7.3	5 - 10	1.8	-	-	-
Parents n (M/F)		**39 (17/22)**			**61 (29/32)**		-	-	-
Age (years)	40.02	22.94 - 60.92	9.82	44.93	28.38 - 63.19	7.33	-2.67	65.35	**0.010**
FSIQ	115.1	96 - 136	9.8	111.0	86 - 136	10.9	1.92	98	*0.058*
VIQ	111.4	91 - 138	12.5	108.5	84 - 130	10.2	1.26	98	0.210
PIQ	114.8	91 - 148	10.3	111.0	77 - 137	11.9	1.64	98	0.104

Bold indicates significance $p < .05$; Italics indicates unequal variance assumed; ^Comparison severity score labels are as follows: 0-2 = "minimal-to-no evidence", 3-4 = "low", 5-7 = "moderate", 8-10 = "high". ADOS, Autism Diagnostic Observation Scale; FSIQ, Full-Scale IQ; PIQ, Performance IQ; RRB, Restricted and Repetitive Behaviors and Interests; SA, social affect; VIQ, Verbal IQ.

Data Processing

Areas of Interests (AOIs). AOIs were manually drawn in Tobii Studio. The AOIs in the Farmland Scene are depicted in *Fig. 2.1B*, and were categorized as either social (e.g., human figures) or non-social (e.g., barn in the background). "Buffer" regions were created identical to prior work, such that each AOI was proportionally expanded by up to 10% of its original size (Anderson, Colombo, & Jill Shaddy, 2006). When social and non-social AOIs overlapped, the final AOI designation was assigned as social

Gaze processing parameters. Eye movements were recorded for both eyes with a sampling rate of 60 Hz. Parameters to account for data loss in working with populations with neurodevelopmental disorders were modeled in line with previous pipelines (Wass et al., 2013). These parameters were consistent with prior work (M. Lee et al., 2019) and the built-in I-VT fixation filter in Tobii Studio as follows—1) fixations were based on the strict average across both eyes; 2) a velocity threshold of 35 degrees per second was established; 3) adjacent fixations were merged if fixations were less than 100 ms apart and angles were less than 0.5 degrees apart; 4) missing data were linearly interpolated based on a 150 ms maximum continuous gap; and 5) noise reduction was addressed by utilizing a moving average window of 3 samples. Finally, following data export, fixations were set to be a minimum duration of 100 ms (i.e., fixation durations less than 100 ms were excluded).

Quality control procedures. Track loss was based on prior work such that participants' data were excluded if their overall fixation count on the Farmland Scene was < 5 and the total fixation duration was < 4 seconds (i.e., gaze data was reliably collected for at least half of the 8 seconds that the stimulus was presented). These criteria resulted in the exclusion of 17% ASD (n

= 5), 6% control (n = 2), 18% ASD-parent (n = 13) and 13% control parent (n = 6) participants' data. Fisher's Exact Test (FET) and Chi-Squared Test revealed no significant group differences in the proportion of valid or invalid data in ASD versus controls (FET $p = .233$) or in ASD parents versus control parents ($X^2(1, 119) = .374, p = .541$), respectively. The final sample was as follows: n = 29 in the ASD group, n = 34 in the control group, n = 61 in the ASD parent group, and n = 39 in the control parent group. From the sample of parents of individuals with ASD, 24 were characterized as BAP(+) (i.e., meeting criteria for having BAP traits), and 37 were characterized as BAP(-) (i.e., not meeting criteria for the BAP).

Eye-tracking variables (Table 2.2)

Standard gaze variables: Dwell time and fixation count were included in an existing study (Lee et al., 2019), and re-reported here for the purpose of examining the efficacy of more nuanced eye-tracking variables in relation to the overall gaze variables. The below metrics are thought to reflect attentional engagement as well as processing time (Eckstein et al., 2017).

(1) Dwell time—Percentage of looking time (sec) toward an AOI was derived by summing the fixation duration of each AOI and dividing it by the total duration of looking, multiplied by 100.

(2) Fixation count—Percentage of the number of fixations was captured by summing the total number of fixations toward an AOI out of the total number of fixations across the duration of stimulus presentation, multiplied by 100.

Dwell time patterns:

(3) First fixation duration—The first fixation duration on an AOI (social or non-social) was derived by measuring the time (in sec) spent examining the AOI during the first fixation before making a fixation transition. This variable reflects how much either social or non-social information initially attracted attention.

(4) Fixations over time—Growth curve analyses (GCA) were employed to investigate change in looking patterns over the course of the stimulus presentation towards social versus non-social AOIs, adapted from the *EyetrackingR* package (Dink & Ferguson, 2015). To account for track loss at the end of the image as well as pre-established attention-capturing stimuli (i.e., center and corner crosshairs) prior to stimulus presentation, 7 seconds of the 8 second image were examined (500 ms removed from the beginning and end of the stimuli), using 1 second time bins. Follow-up analyses examined the divergence between groups of social versus non-social looking using t-tests that are embedded within the divergence vignette from the *EyetrackingR* package (Dink & Ferguson, 2015). 300 ms time bins were used for divergence analyses given that the average fixation duration was 300 ms across participants.

Fixation patterns:

(5) Percentage of perseverative fixations were explored as a means to tap into attentional "stickiness" or mental disengagement (Hughes & Russell, 1993), and were derived by summing fixations that occurred in succession toward the same AOI, divided by the total number of fixations, multiplied by 100.

(6) Percentage of regressive fixations were captured as the percentage of times a participant returned their gaze to a specific AOI that had already been previously explored. This

was determined by summing the number of fixations that occurred towards an AOI previously fixated (not including successive fixations/perseverative fixations), divided by the total number of fixations, multiplied by 100. Regressive fixations is thought to reflect slower processing speed or the loss of mental set/executive control (R. W. Booth & Weger, 2013; Perea & Carreiras, 2003; Rayner, 1998; Rayner et al., 2010). It can also reflect which AOIs repeatedly attracted the participants' attention.

(7) Exploration AOI—To investigate how much participants explored either social of non-social AOIs, the number of fixations per track time (in sec) toward social or non-social information was further explored. Greater exploration reflects a larger number of fixations toward social or non-social information for a given second, and provides a general indication of attentional capacity and cognitive load (Zagermann, Pfeil, & Reiterer, 2018).

(8) Percentage of first fixation AOI—The percentage of first fixations toward social or non-social information was measured by summing the total number of first fixations that was social or non-social and dividing it by the total number of first fixations, multiplied by 100. First fixation AOI is thought to index the utilization of peripheral visual information, that is associated with global or rapid and automatic visual information processing and generally reflects visual information preference (Kimchi, 1992).

(9) Transition entropy analysis—exploring the transitions between different AOIs provides an estimate of general exploration. This method of analyses has also been shown to reflect shifts in attention (Luna et al., 2008), in addition to reasoning abilities through the process of comparison between task relevant and task irrelevant information (Demarais & Cohen, 1998; Thibaut & French, 2016; Vigneau, Caissie, & Bors, 2006). For the purpose of this study, to

demonstrate the utility of examining transitions, we explored the transitions between social and non-social information in five ways: i) social to social AOI transitions, ii) non-social to non-social AOI transitions, iii) social to non-social AOI transitions, iv) non-social to social AOI transitions, and v) total transitions between social and non-social AOIs. Percentages based on the total number of transitions information were calculated for i) – iv). For the final variable, a percentage was calculated by taking the total number of transitions between social and non-social AOIs (regardless of direction) divided by the total number of fixations, multiplied by 100.

Distribution patterns:

(10) Coverage exploration—in order to obtain a general measure of coverage, exploration regardless of AOI type was examined. As such, the total number of fixations per participant was divided by the total time spent examining the scene, to produce the number of fixations that occurred per second of track time regardless of AOI. A higher number indicates a greater number of fixations occurring per second of track time, reflecting greater exploration.

(11) Spatial distribution or coverage analyses (*Fig. 2*) was conducted to obtain an estimate of how much of the screen was being explored regardless of social or non-social AOI. Given that the Tobii T60 screen was 1,280 x 1,024 pixels, a 5 x 4 matrix of 20 large areas (256 x 256 pixels / 6.45° x 6.45°) and a 10 x 8 matrix of 80 small areas (128 x 128 pixels / 3.2° x 3.2°) were generated. Based on prior work (Hessels, Kemner, van den Boomen, & Hooge, 2016) showing that the attention maintaining and capturing abilities of an AOI increases with size but asymptotes at 3° visual angle (i.e., 120 x 120 pixels using the T60 Tobii display) for ASD and control groups, the smaller area 10 x 8 matrix would be the most appropriate for the present

study while still maintaining equal sized “boxes”. Note, the step below the smaller areas utilized here (i.e., 64 x 64 pixels), would result in AOIs that fell about half (1.6° x 1.6°) the ideal AOI size according to this prior work (Hessels et al., 2016), and would impact the AOI’s ability to capture and maintain the participants’ attention. As such, we present both the ideal smaller and larger grids for methodological purposes. Each fixation point’s location was categorized into one of these 20 or 80 “boxes”, respectively. To account for the different number of fixations per participant, the percentage of mini areas explored was computed per participant by taking the number of areas explored and dividing it by the total number of fixations for that participant, which was then multiplied by 100. This final percent coverage was included in subsequent analyses for larger (5 x 4 matrix) and smaller (10 x 8 matrix) areas. A higher percentage represents greater coverage overall (i.e., a greater proportion of fixations were covering unique areas not previously explored), while a lower percentage indexes less coverage or scatter. This measure indicates whether visual attention was “trapped” within certain general regions of a stimulus, or whether there is greater flexibility in underlying attentional mechanisms.

Table 2.2: Definitions eye-tracking variables

Variable	Variable Definition
Overall gaze variables	
Dwell time	Derived by summing the fixation duration of each AOI and dividing it by the total duration of looking, multiplied by 100.
Percentage of fixation count	Captured by summing the total number of fixations toward an AOI out of the total number of fixations across the duration of stimulus presentation, multiplied by 100.
Dwell time patterns	
First fixation duration	Derived by measuring the time (in sec) spent examining the AOI during the first fixation before making a fixation transition.
Fixations over time	Growth curve analyses (GCA) were employed to investigate change in looking patterns over the course of the stimulus towards social versus non-social AOIs. To account for track loss at the beginning and end of the stimulus presentation, 7 seconds of the 8 second image were examined (500 ms removed from the beginning and end of the stimuli), using 1 second time bins. Follow-up analyses examined the divergence between groups of social versus non-social looking using t-tests with 300 ms time bins.
Fixation patterns	
Percentage of perseverative fixations	Derived by summing fixations that occurred in succession toward the same AOI, divided by the total number of fixations, multiplied by 100.
Percentage of regressive fixations	Determined by summing the number of fixations that occurred towards an AOI previously fixated (not including successive fixations/perseverative fixations), divided by the total number of fixations, multiplied by 100.
Exploration AOI	The number of fixations per track time (in sec) toward social or non-social information was calculated.
Percentage of first fixation AOI	The total number of first fixations that was social or non-social were summed and dividing it by the total number of first fixations, multiplied by 100.

Transition entropy analysis	Transitions between social and non-social information were explored in five ways: i) social to social AOI transitions, ii) non-social to non-social AOI transitions, iii) social to non-social AOI transitions, iv) non-social to social AOI transitions, and v) total transitions between social and non-social AOIs. Percentages based on the total number of transitions information were calculated for i) – iv). For the final variable, a percentage was calculated by taking the total number of transitions between social and non-social AOIs (regardless of direction) divided by the total number of fixations, multiplied by 100.
Distribution patterns	
Coverage exploration	The total number of fixations per participant was divided by the total time spent examining the scene, to produce the number of fixations that occurred per second of track time regardless of AOI.
Spatial distribution/coverage analyses	First, a 5 x 4 matrix of 20 large areas (256 x 256 pixels / 6.45° x 6.45°) and a 10 x 8 matrix of 80 small areas (128 x 128 pixels / 3.2° x 3.2°) were generated. . Each fixation point's location was categorized into one of these 20 or 80 "boxes", respectively. To account for the different number of fixations per participant, the percentage of mini areas explored was computed per participant by taking the number of areas explored and dividing it by the total number of fixations for that participant, which was then multiplied by 100. This final percent coverage was included in subsequent analyses for larger (5 x 4 matrix) and smaller (10 x 8 matrix) areas.

Figure 2.2. *Schematic representing fixation distribution scatter/coverage analysis AOIs. A) large areas (5 x 4 grid) and B) small areas (10 x 8 grid).*

Statistical Analysis

Assumptions testing.

Data were examined to ensure model assumptions of primary statistical tests (i.e., multivariate analysis of variance; MANOVA) were met. Gaze variables for social and non-social looking were included in assumptions testing, and were conducted separately for proband and parent groups. All assumptions were adequately met as follows: 1) two or more dependent variables are

measured at the interval or ratio level; 2) independent variables consist of two categorical, related groups; 3) there exists independence of observations as each participant belongs to only one group; 4) sample size is adequate for a MANOVA; 5) no participant fell 3 SD above or below the mean for proband or parent groups; 6) residual errors were all normally distributed based on examination of Q-Q plots, and outcome variables were mostly normally distributed based on histograms and Shapiro-Wilk's test (with the exception of non-social dwell time in parents and perseveration across parent and proband groups); 7) social and non-social variables were co-linear such that significant negative correlations emerged for proband groups (rs > -.72, ps < .0001) and parent groups (rs < -.67, ps < .0001). The 8th assumption, which assumes that there is homogeneity of variance-covariance matrices, was violated for some variables. For parents, dwell time and perseveration towards social or non-social information violated Box's M test. The Levene's test was used as a follow-up test of homogeneity of variance, showing no signs of test of sphericity violations across variables. Box's M tests were also marginally significant for proband groups, with perseveration towards social or non-social information violating the assumption. Follow-up Levene's test demonstrated that non-social looking patterns violated the test of sphericity. As such, across all variables, findings using the more robust Pillai's Trace (Olson, 1974) are reported. Finally, none of the dependent variables are multicollinear with no correlation coefficient > .90.

Group differences.

All group differences in overall gaze variables, fixation patterns, and time to first fixation variables were examined using a one-way MANOVA separately for parent and proband groups.

Only significant MANOVAs were followed up with univariate ANOVAs. For BAP-level differences, additional planned post-hoc pairwise comparisons (i.e., BAP+ versus BAP- versus parent control groups) were conducted when the overall MANOVA or univariate ANOVAs were significant. Given that the percentage of perseverations towards social and non-social information was skewed, MANOVA results were followed up with non-parametric Mann-Whitney U tests. To examine gaze variables not involving social and non-social AOIs (i.e., distribution patterns), one-way ANOVAS were conducted separately for proband and parent groups.

Due to their lower sample sizes and categorical nature, first fixation duration and AOIs were analyzed using independent samples t-tests and chi-squared, respectively. Because sample sizes were low (only n = 6 probands and n = 17 parents) for first fixations towards non-social information, only group differences examining time spent first fixating on social information were conducted. Independent samples t-tests to examine group differences were conducted separately for probands and parents, and for participants whose first fixations were towards social information. Because sample sizes are smaller for non-social first fixations, a series of 2 X 2 contingency tables using Fisher's exact tests were performed separately in parent and proband groups to examine group differences in the proportions of first fixations that were directed towards social and non-social information.

To investigate changes in looking patterns towards social versus non-social AOIs over the course of the stimulus presentation, GCA were utilized using similar methods applied in recent work (Winston et al., 2020). Specifically, orthogonal polynomial terms, each representing a different pattern of looking, were added in a stepwise fashion. The linear term reflected an

increase or decrease in proportion of looking over time linearly, the quadratic term reflected the dynamic nature of switching from one AOI to another and back again, and finally, the cubic term reflected the timing of switches between AOIs. Only interactions that include a polynomial term were reported.

Results

Detailed statistical analyses are reported in Tables 2.3 – 2.4.

Overall gaze variables (*Fig. 2.3*)

Despite the sample between studies overlapping completely, the below overall gaze variables findings applied different statistical analyses than those applied in Lee et al. (2019).

(1) Dwell time:

Probands. Overall, there were no sig nificant differences between the ASD and control group in the percentage of time spent attending towards social or non-social information ($F_{(2,53)}$ = 1.40, Pillai's Trace = .05, p = .255, partial η^2 = .050).

Parents. Trending differences emerged in the multivariate test between parents across social and non-social looking ($F_{(2,97)}$ = 2.80, Pillai's Trace = .06, p = .066, partial η^2 = .055).

BAP. The overall model for social and non-social looking times were significant across BAP+, BAP-, and parent controls ($F_{(4,197)}$ = 2.71, Pillai's Trace = .11, p < .05, partial η^2 = .053), significant differences emerging in both social ($F_{(2,97)}$ = 3.70, p < .05, partial η^2 = .071) and non-social ($F_{(2,97)}$ = 4.44, p < .05, partial η^2 = .084) looking time. Pairwise comparisons revealed that BAP+ parents showed significantly reduced social looking compared to the parent control group (mean difference = -8.77, p < .01) and increased non-social looking compared to both BAP- parents (mean difference = 5.51, p < .05) and parent controls (mean difference = 6.84, p < .05).

(2) Percentage of fixation count:

Probands. No significant group differences emerged in the percentage of fixations directed towards social or non-social information ($F_{(2,53)} = .65$, Pillai's Trace = .02, $p = .524$, partial $\eta^2 = .024$).

Parents. Similarly, no differences emerged between parent groups ($F_{(2,97)} = 1.98$, Pillai's Trace = .04, $p = .144$, partial $\eta^2 = .039$).

BAP. No differences in BAP status emerged overall for social or non-social looking ($F_{(4,194)} = 1.42$, Pillai's Trace = .06, $p = .229$, partial $\eta^2 = .028$).

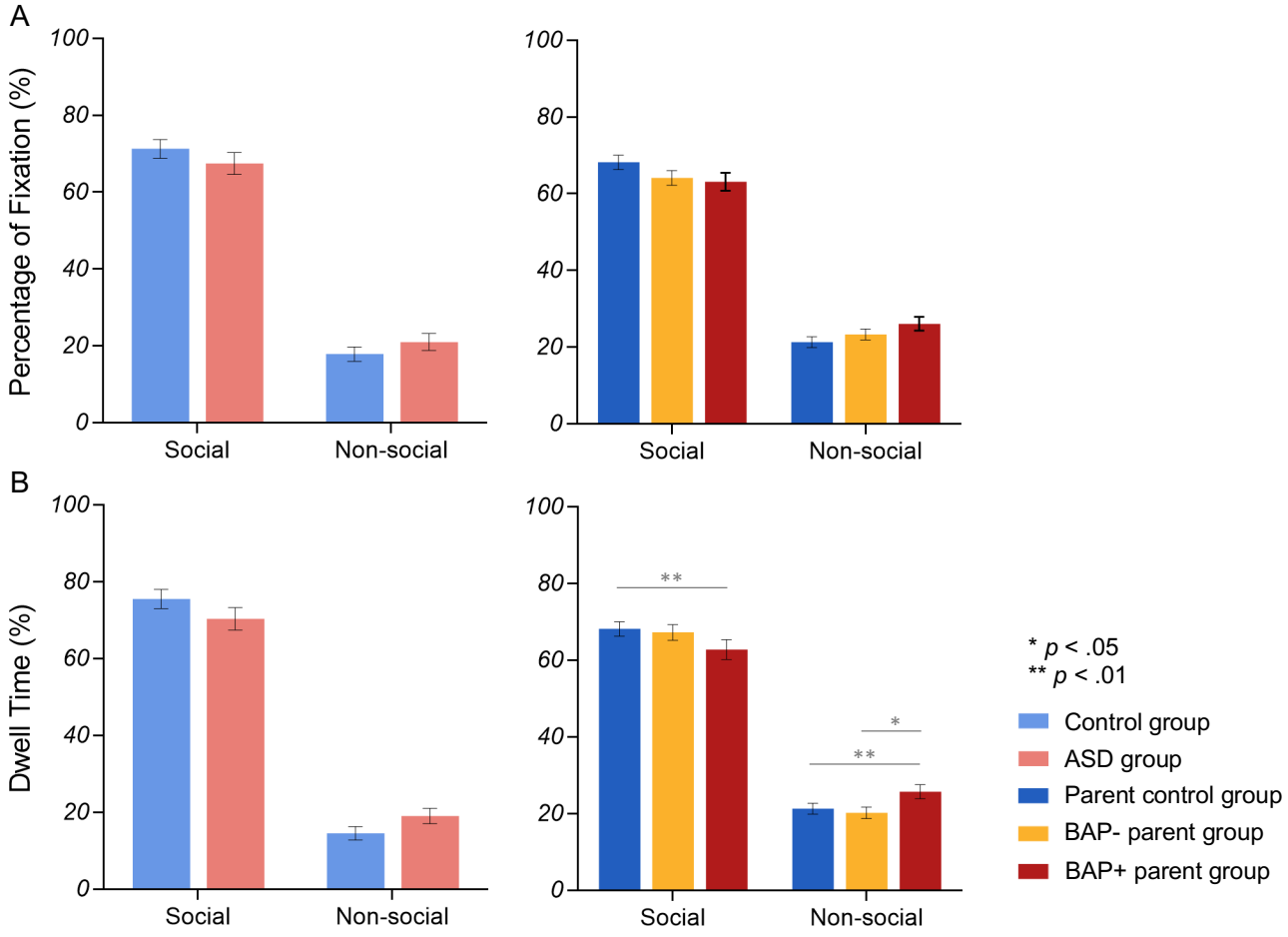

Figure 2.3. *Overall gaze variables depicting A) fixation count and B) dwell time. Significant differences between BAP(+) and Control parent groups emerged in dwell time across social and non-social visual attention.*

Table 2.3: *Summary of Result - ASD versus control groups*

	Control Group	**ASD Group**	**Group Differences**				
	M (SD)	M (SD)	*F*	*Pillai's Trace*	*df*	*p*	partial η^2
Overall Gaze Variables							
Dwell Time (%) - social	75.54 (12.41)	70.37 (16.21)	1.40	0.05	2, 53	0.255	0.050
Dwell Time (%) - non-social	14.54 (7.32)	19.03 (12.63)					
Percentage of Fixations - social	71.25 (12.63)	67.46 (15.74)	0.65	0.02	2, 53	0.524	0.024
Percentage of Fixations - non-social	17.85 (7.98)	21 (13.42)					
Dwell Time Patterns			*t*	-	*df*	*p*	-
First Fixation Duration (s) - social	2.96 (1.67)	2.58 (1.13)	0.90	-	40	0.375	-
Fixation Patterns			-	-	-	*Fisher's Exact Test*	-
First Fixation AOI (%) - social	85.7	90.5	-	-	-	0.688	-
First Fixation AOI (%) - non-social	14.3	9.5	-	-	-		-
Perseverative Fixations (%) - social*	74.18 (30.88)	65.05 (35.51)	**3.27**	**0.11**	**2, 53**	**0.046**	**0.110**
Perseverative Fixations (%) - non-social*	7.08 (14.94)	23.4 (32.13)					
Regressive Fixations (%) - social	71.01 (12.43)	67.22 (16.43)	0.62	0.02	2, 53	0.541	0.023
Regressive Fixations (%) - non-social	18.09 (8.77)	21.3 (13.54)					
Exploration AOI (fix/s) - social	3.1 (0.59)	3.37 (0.7)	1.51	0.06	2, 53	0.231	0.055
Exploration AOI (fix/s) - non-social	4.33 (1.05)	4.09 (1.47)					
Transition Entropy Total (%)	79.52 (16.58)	78.33 (16.60)	0.07	-	1, 55	0.791	0.001
Social to social (%)	64.86 (17.87)	59.48 (23.70)					
Non-social to non-social (%)	4.26 (6.59)	7.44 (7.87)	0.979	0.053	3, 52	0.41	0.053
Social to non-social (%)	15.71 (9.50)	16.43 (9.10)					
Non-social to social (%)	15.18 (6.52)	16.65 (10.24)					

Bold values indicate significance at $p < .05$; *Non-parametric Mann-Whitney *U* results are presented in the body of the manuscript

Table 2.4: *Summary of Result - ASD parent versus parent control groups*

	Parent Control Group	**ASD Parent Group**	**Group Differences**				
	M (SD)	M (SD)	*F*	*Pillai's Trace*	*df*	*p*	partial η^2
Overall Gaze Variables							
Dwell Time (%) - social	71.57 (13.95)	65.5 (11.67)	2.80	0.06	2, 97	0.066	0.055
Dwell Time (%) - non-social	18.87 (10.05)	22.36 (8.76)					
Percentage of Fixations - social	68.17 (13.27)	63.71 (10.24)	1.98	0.04	2, 97	0.144	0.039
Percentage of Fixations - non-social	21.28 (9.33)	24.38 (8.46)					
Dwell Time Patterns			*t*	-	*df*	*p*	-
First Fixation Duration (s) - social	2.45 (1.17)	3.07 (1.60)	-1.66	-	63	0.102	-
Fixation Patterns			-	-	-	*Fisher's Exact Test*	-
First Fixation AOI (%) - social	77.40	80.40	-	-	-	0.784	-
First Fixation AOI (%) - non-social	22.60	19.60	-	-	-		-
Perseverative Fixations (%) - social*	72.83 (30.64)	62.8 (33.78)	1.50	0.03	2, 97	0.228	0.030
Perseverative Fixations (%) - non-social*	17.89 (23.93)	18 (22.19)					
Regressive Fixations (%) - social	68.5 (13.69)	63.44 (10.44)	2.31	0.05	2, 97	0.104	0.046
Regressive Fixations (%) - non-social	21.5 (9.61)	24.8 (8.92)					
Exploration AOI (fix/s) - social	3.25 (0.64)	3.34 (0.68)	0.84	0.02	2, 97	0.434	0.017
Exploration AOI (fix/s) - non-social	4.08 (0.96)	3.86 (1.13)					
Transition Entropy Total (%)	80.44 (14.05)	77.03 (15.49)	1.24	-	1, 99	0.269	0.012
Social to social (%)	58.37 (16.46)	53.45 (14.13)					
Non-social to non-social (%)	6.84 (7.77)	8.95 (7.95)	1.02	0.031	3, 96	0.387	0.031
Social to non-social (%)	17.70 (7.42)	18.75 (7.32)					
Non-social to social (%)	17.09 (7.52)	18.85 (7.28)					

Bold values indicate significance at $p < .05$; *Non-parametric Mann-Whitney *U* results are presented in the body of the manuscript

Dwell time patterns (*Fig. 2.4)*

(3) First fixation duration:

Probands. The ASD group did not differ from the control group in the duration of their first social AOI fixation ($t_{(40.10)}$ = .90, p = .375).

Parents. There were no significant group differences in the time spent initially fixating on social information ($t_{(63)}$ = -1.66, p = .102).

BAP. Similarly, there were no significant group differences between BAP+ and parent control groups ($t_{(39)}$ = -1.34, p = .188), BAP+ and BAP- groups ($t_{(46)}$ = -1.61, p = .114), and BAP- and parent control groups ($t_{(39)}$ = .002, p = .999) in the time spent first fixating on social information.

(4) Fixations over time (Table 2.5):

Probands. There were no significant group differences detected across linear (*Estimate* = .10, t(832) = .75, p = .453), quadratic (*Estimate* = .21, t(832) = 1.58, p = .12), or cubic (*Estimate* = .006, t(832) = .05, p = .962) terms in social versus non-social looking patterns over the course of the stimulus presentation. Visually, it appears that individuals with ASD disengage from social information early, decreasing over time, while the control group evidences increased social looking initially, that also decreases over the course of the task. Follow-up time-bin divergence analyses revealed significant differences occurring halfway through the stimulus presentation, showing that individuals with ASD demonstrated reduced social looking between 3000 and 3300 ms compared to controls.

Parents. In contrast, a significant group difference was detected for the cubic polynomial term (*Estimate* = -.23, $t(1474) = -2.24$, $p < .05$), indicating that the ASD parent group shifts away earlier from social AOIs, and demonstrates decreased attention to social information over time compared to the parent control group. Follow-up time-bin divergence analyses demonstrated differences primarily occurring during the beginning (i.e., 300 - 600 ms) and end (i.e., 4500 - 4800 ms and 6900 - 7200 ms) of the stimulus presentation, such that ASD parents showed reduced social looking patterns compared to controls. Interestingly, ASD parents also demonstrated increased social looking relative to the parent control group between 5100 - 5400 ms, showing a dynamic pattern of an initial decrease, then increase, then decrease in social looking towards the end of the stimulus presentation, compared to the parent control group.

BAP. A significant group difference was detected for the linear, quadratic, and cubic terms, indicating that BAP+ parents shifted away earlier, and demonstrated decreased social attention over the course of the task compared to the BAP- (*linear estimate* = .46, $t(1474) = 3.38$, $p < .001$; *quadratic estimate* = .48, $t(1474) = 3.50$, $p < .001$, *cubic estimate* = .30, $t(1474) = 2.28$, $p < .05$) and parent control groups (*linear estimate* = .44, $t(1474) = 3.31$, $p < .001$; *quadratic estimate* = .39, $t(1474) = 2.91$, $p < .001$, *cubic estimate* = .42, $t(1474) = 3.20$, $p = .001$). BAP- and parent control groups did not differ from one another across any linear, quadratic, or cubic terms (*linear estimate* = -.02, $t(1474) = -.16$, $p = .876$; *quadratic estimate* = -.09, $t(1474) = -.76$, $p = .446$, *cubic estimate* = .11, $t(1474) = .10$, $p = .320$). Divergence tests showed that the BAP+ group fixated more towards social information relative to the parent control group towards the send half of the stimulus presentation (i.e., 5100 - 5400 ms), showing a sudden decrease towards the end (i.e., 6900 - 7200 ms). Similarly, the BAP+ group showing significantly decreased social

attention towards the end of the stimulus compared to the BAP- parent group between 6900 - 7200 ms. In contrast, the BAP- group showed reduced social attention towards the second half of the stimulus presentation (i.e., 4500 -4800 ms), with a later (i.e., 5100 - 5400) increase in social attention relative to controls.

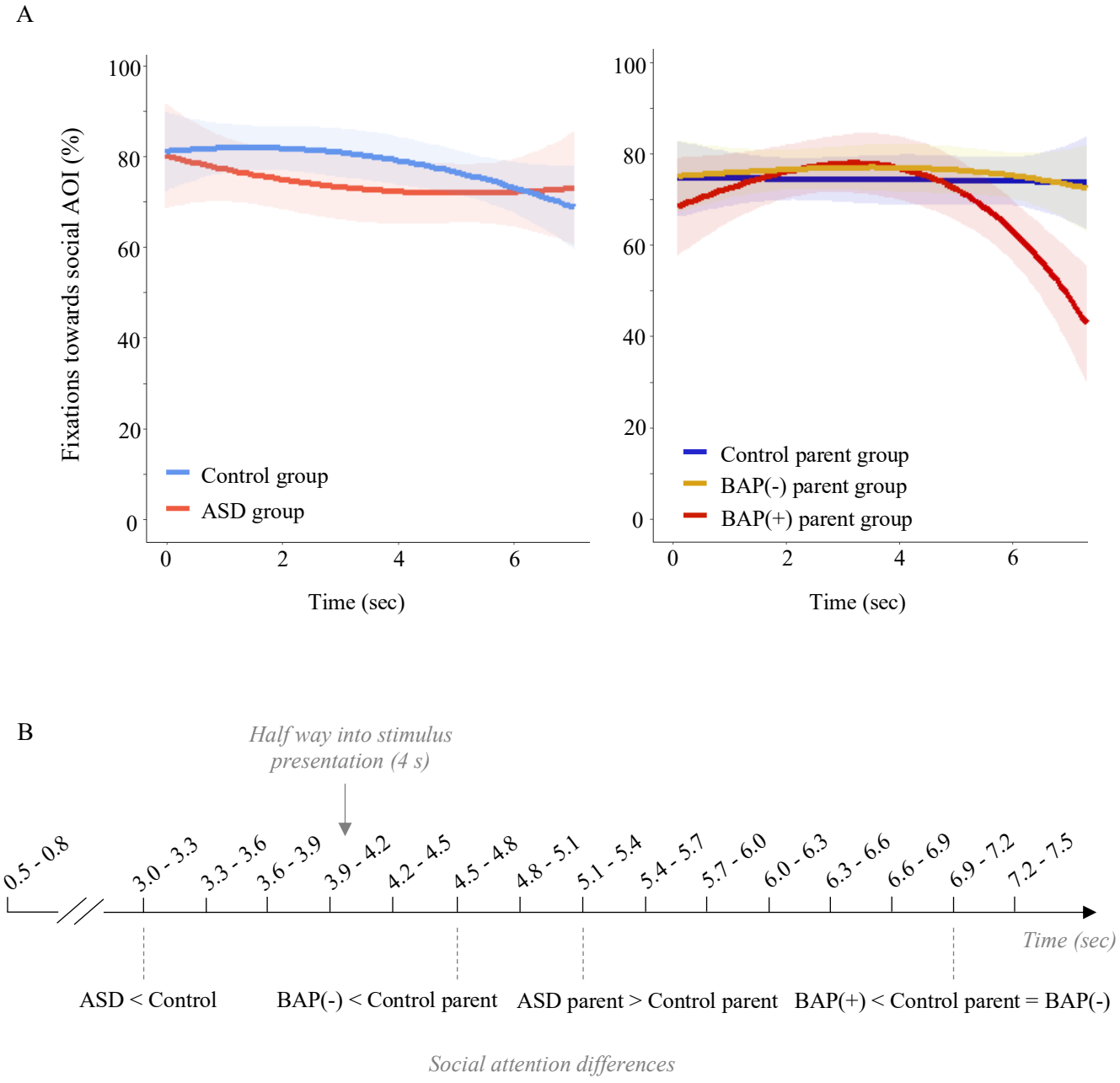

Figure 2.4. *Dwell time patterns depicting A) proportion of fixations over time (higher value indicates greater social attention) and B) a schematic representing divergence time-bin analyses, where individuals with ASD were observed to attend less to social information than the control group half way into the stimulus presentation. Both BAP(-) and BAP(+) parents showed a spike in social attention around 5 seconds, with the BAP(+) group showing a striking decrease in social attention towards the end of the stimulus presentation compared to BAP(-) and Control parent groups.*

Table 2.5: *Summary of Results for GCA analyses - Fixations over time*

	Control > ASD		
	Estimate	*t*	*p*
Intercept	**-0.74**	**-30.42**	**< .0001**
Linear	-0.10	-0.75	0.453
Quadratic	-0.21	-1.58	0.120
Cubic	-0.01	-0.05	0.962

	Parent control > ASD parent		
	Estimate	*t*	*p*
Intercept	**-0.72**	**-44.73**	**< .0001**
Linear	0.16	1.53	0.126
Quadratic	0.10	0.92	0.360
Cubic	**0.23**	**2.24**	**0.025**

	Parent control > BAP+			Parent control > BAP-			BAP- > BAP+		
	Estimate	*t*	*p*	*Estimate*	*t*	*p*	*Estimate*	*t*	*p*
Intercept	**-0.08**	**-0.26**	**0.010**	-0.15	-0.54	0.590	**-0.07**	**-2.08**	**0.038**
Linear	**0.44**	**3.31**	**0.001**	-0.02	-0.16	0.876	**0.46**	**3.38**	**0.001**
Quadratic	**0.39**	**2.91**	**0.004**	-0.09	-0.76	0.446	**0.48**	**3.50**	**0.001**
Cubic	**0.42**	**3.20**	**0.001**	0.11	0.10	0.320	**0.30**	**2.28**	**0.023**

Bold values indicate significance at $p < .05$

Fixation patterns (Fig. 2.5 - 2.7)

(5) Percentage of first fixation AOI:

Probands. Fisher's Exact test revealed no significant differences in first fixations towards social (*ASD* 39%, *Control* 49%) and non-social information (*ASD* 4%, *Control* 8%) between groups (p = .688).

Parents. Similarly, no differences emerged between first fixation looks to social (*ASD parent* 50%, *Parent control* 29%) versus non-social (*ASD parent* 12%, *Parent control* 9%) information between parent groups (p = .784).

BAP. Similarly, no differences emerged when considering BAP status in parents in the proportion of social (*BAP+* 21%, *BAP-* 29%, *parent control* 29%) and non-social (*BAP+* 2%, *BAP-* 10%, *Parent control* 9%) first fixations.

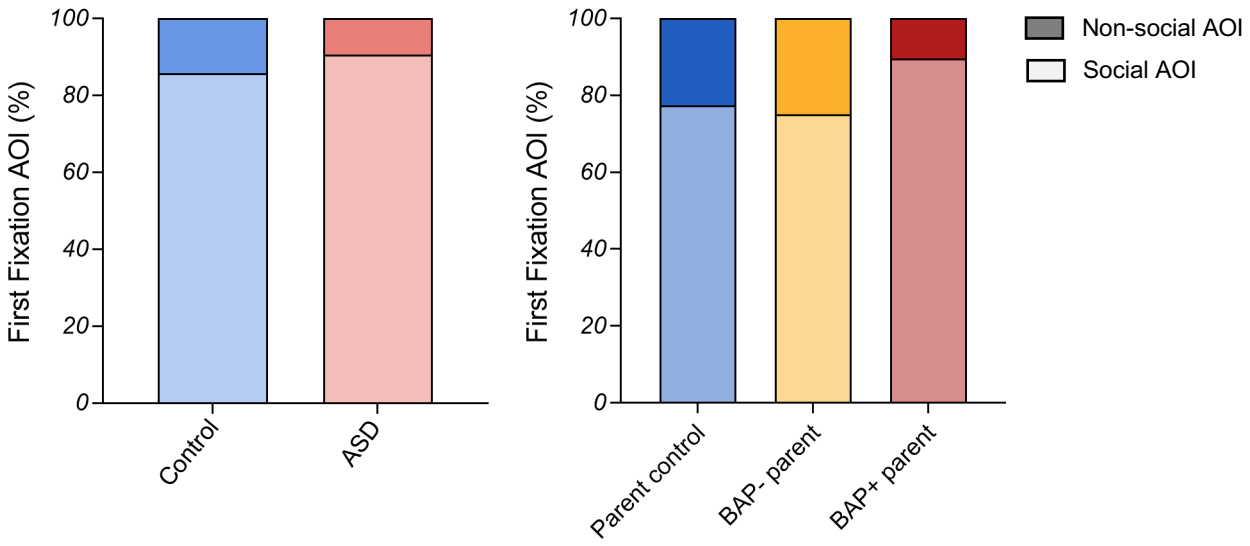

Figure 2.5. *First fixation AOI showing both percentage of first fixations that were made towards social information (lighter shade) and non-social information (darker shade).*

(6) Percentage of perseverative fixations *(Fig 2.6A):*

Probands. MANOVA results revealed significant differences between ASD and control groups in the percentage of perseverative fixations towards social/non-social information ($F_{(2,53)}$ = 3.27, Pillai's Trace = .11, $p < .05$, partial $\eta^2 = .110$). Follow-up univariate ANOVA tests revealed that the ASD group made a greater proportion of perseverations on non-social information compared to the control group ($F_{(1,54)} = 6.43$, $p < .05$, partial $\eta^2 = .106$). Follow-up non-parametric analyses demonstrated significant group differences in non-social perseverations, showing elevated perseverations towards non-social information in the ASD ($M_{rank} = 32.98$) versus control ($M_{rank} = 25.14$) group ($U = 276.5$, $p < .05$). No significant differences emerged between groups for social perseverations (*ASD* $M_{rank} = 26.13$, *Control* $M_{rank} = 30.28$, $U = 327$, $p = .324$).

Parents. No significant group differences were found between ASD parent and parent control groups ($F_{(2,97)} = 1.50$, Pillai's Trace = .03, $p = .228$, partial $\eta^2 = .030$). Non-parametric analyses additionally revealed a comparable percentage of perseverative fixations towards both social (*ASD parent* $M_{rank} = 47.01$, *Parent control* $M_{rank} = 55.96$) and non-social (*ASD parent* $M_{rank} = 50.97$, *Parent control* $M_{rank} = 49.77$) information between groups ($U = 976.5$, $p = .122$ and $U = 1161$, $p = .827$, respectively).

BAP. MANOVA results showed no difference in social or non-social perseverative looking patterns between BAP+, BAP-, or parent control groups ($F_{(4,194)} = 1.59$, Pillai's Trace = .06, $p = .179$, partial $\eta^2 = .032$). However, Mann-Whitney U test revealed that the BAP+ group ($M_{rank} = 26.31$) made significantly fewer perseverations towards social information compared to the parent control group ($M_{rank} = 35.50$) ($U = 331.5$, $p < .05$).

(7) Percentage of regressive fixations *(Fig 2.6B):*

Probands. No significant group differences emerged for social/non-social regressive fixations ($F_{(2,53)}$ = .62, Pillai's Trace = .02, p = .541, partial η^2 = .023).

Parents. Parents also showed comparable social and non-social regressive fixations ($F_{(2,97)}$ = 2.31, Pillai's Trace = .05, p = .104, partial η^2 = .046).

BAP. No significant differences emerged by BAP status ($F_{(4,194)}$ = 1.87, Pillai's Trace = .07, p = .118, partial η^2 = .037)

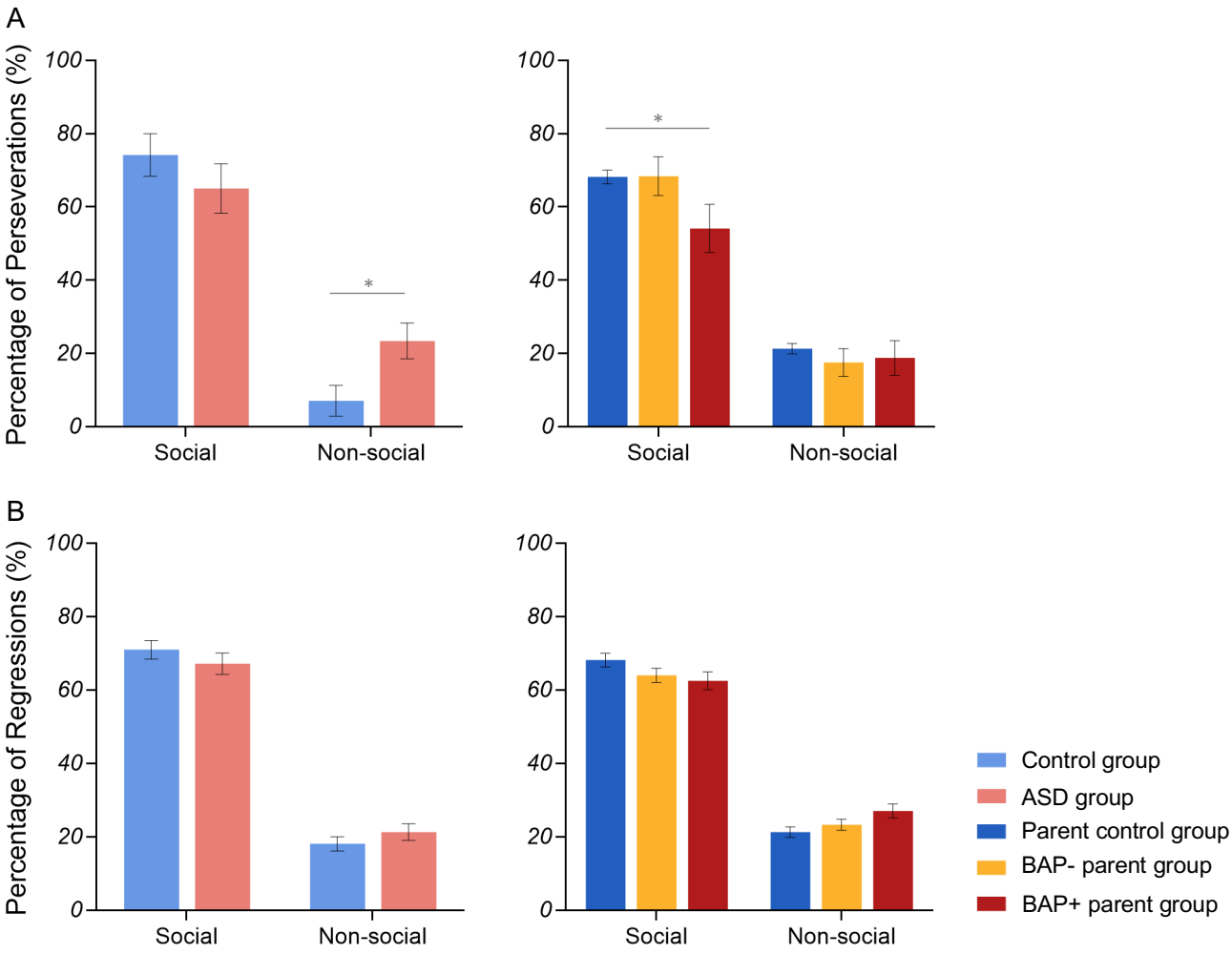

Figure 2.6. *Fixation patterns depicting A) Percentage of perseverative fixations and B) Percentage of regressive fixations. Significant differences between ASD and control groups, and BAP+ and parent control groups emerged in perseverative fixation patterns, showing elevated non-social and reduced social perseverative fixations, respectively.*

(8) Exploration:

Probands. ASD and control groups did not differ in the number of fixations per second of track time made towards social and non-social information ($F_{(2,52)} = 1.51$, Pillai's Trace = .06, $p = .231$, partial $\eta^2 = .055$).

Parents. Similarly, parents did not show significant group differences in exploration towards social and non-social AOIs ($F_{(2,97)} = .84$, Pillai's Trace = .02, $p = .434$, partial $\eta^2 = .017$).

BAP. Similarly, parent findings remained non-significant regardless of BAP status ($F_{(4,194)} = 1.794$, Pillai's Trace = .07, $p = .132$, partial $\eta^2 = .036$).

(9) Transition entropy *(Fig. 2.7):*

Probands. There were no significant differences in the percentage of transitions occurring (regardless of direction of fixation transitions) between social and non-social information ($F_{(3,52)} = .98$, Pillai's Trace = .05, $p = .410$, partial $\eta^2 = .053$). Similarly, there were no significant differences in the percentage of total transitions occurring between social and non-social information between ASD and control groups ($F_{(1,54)} = .07$, $p = .791$, partial $\eta^2 = .001$).

Parents. Likewise, parents showed no differences in the percentage of transitions made between social and non-social stimuli when considering direction of transitions ($F_{(3,96)} = 1.02$, Pillai's Trace = .03, $p = .387$, partial $\eta^2 = .031$), or overall ($F_{(1,98)} = 1.24$, $p = .269$, partial $\eta^2 = .012$).

BAP. BAP status did not affect overall findings across specific transition patterns ($F_{(6,192)} = .72$, Pillai's Trace = .04, $p = .637$, partial $\eta^2 = .022$) and overall ($F_{(2,97)} = .85$, $p = .429$, partial $\eta^2 = .017$).

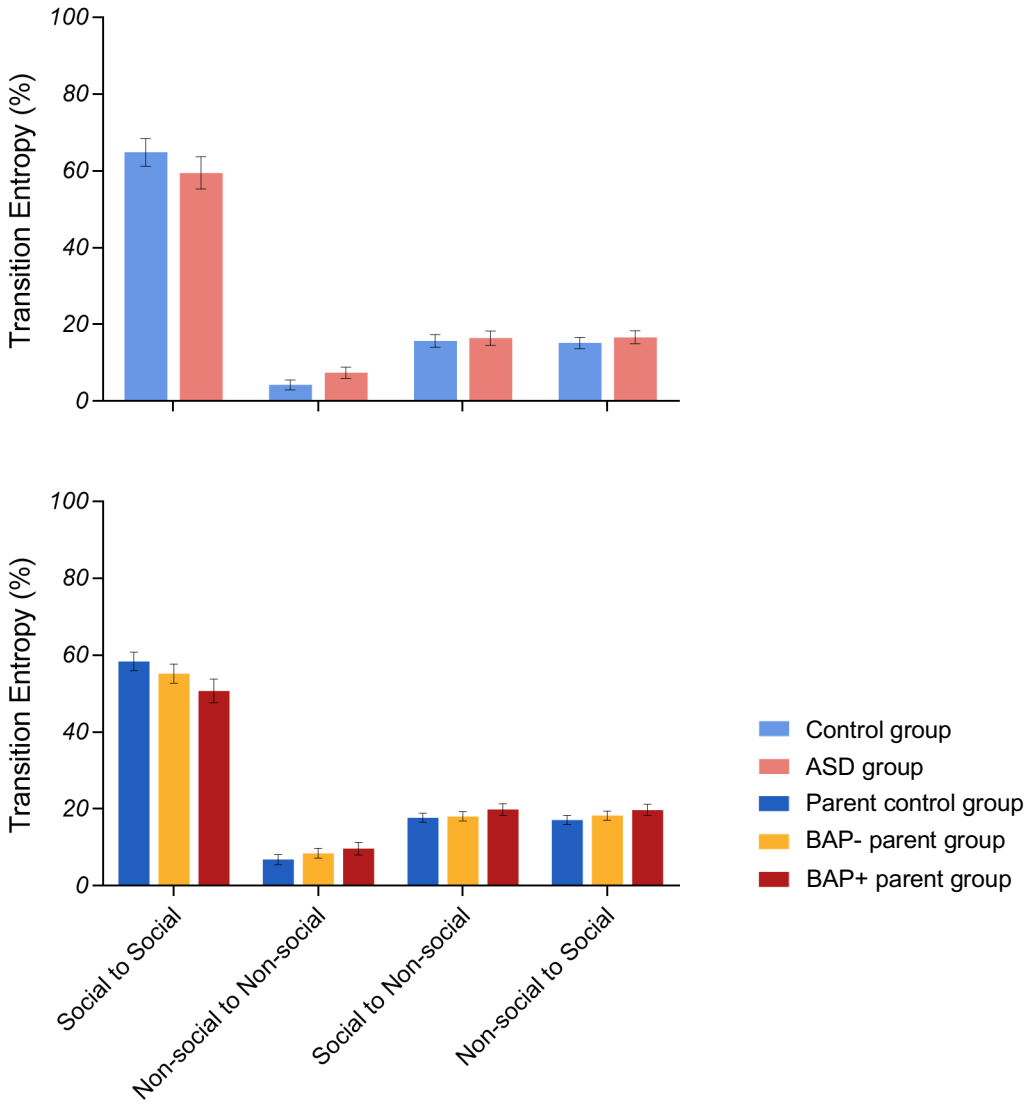

Figure 2.7*. Fixation patterns depicting transition entropy analysis (i.e., the percentage of fixations characterized as transitions from one AOI to another) as follows: social to social AOI, non-social to non-social AOI, social to non-social AOI, and non-social to social AOI transitions.*

Distribution analyses (Fig. 2.8)

(10) Coverage exploration:

<u>*Probands*</u>. The ASD and control groups demonstrated a similar number of fixations per

second of track time regardless of AOI ($F_{(1,54)} = 1.35$, $p = .251$, partial $\eta^2 = .024$).

Parents. Similarly, the ASD parent and the parent control groups showed comparable exploration across the scene ($F_{(1,98)} = .001$, $p = .981$, partial $\eta^2 < .0001$).

BAP. BAP traits did not alter this pattern of comparability, such that no differences across BAP groups and controls emerged overall ($F_{(2,97)} = .17$, $p = .848$, partial $\eta^2 = .003$).

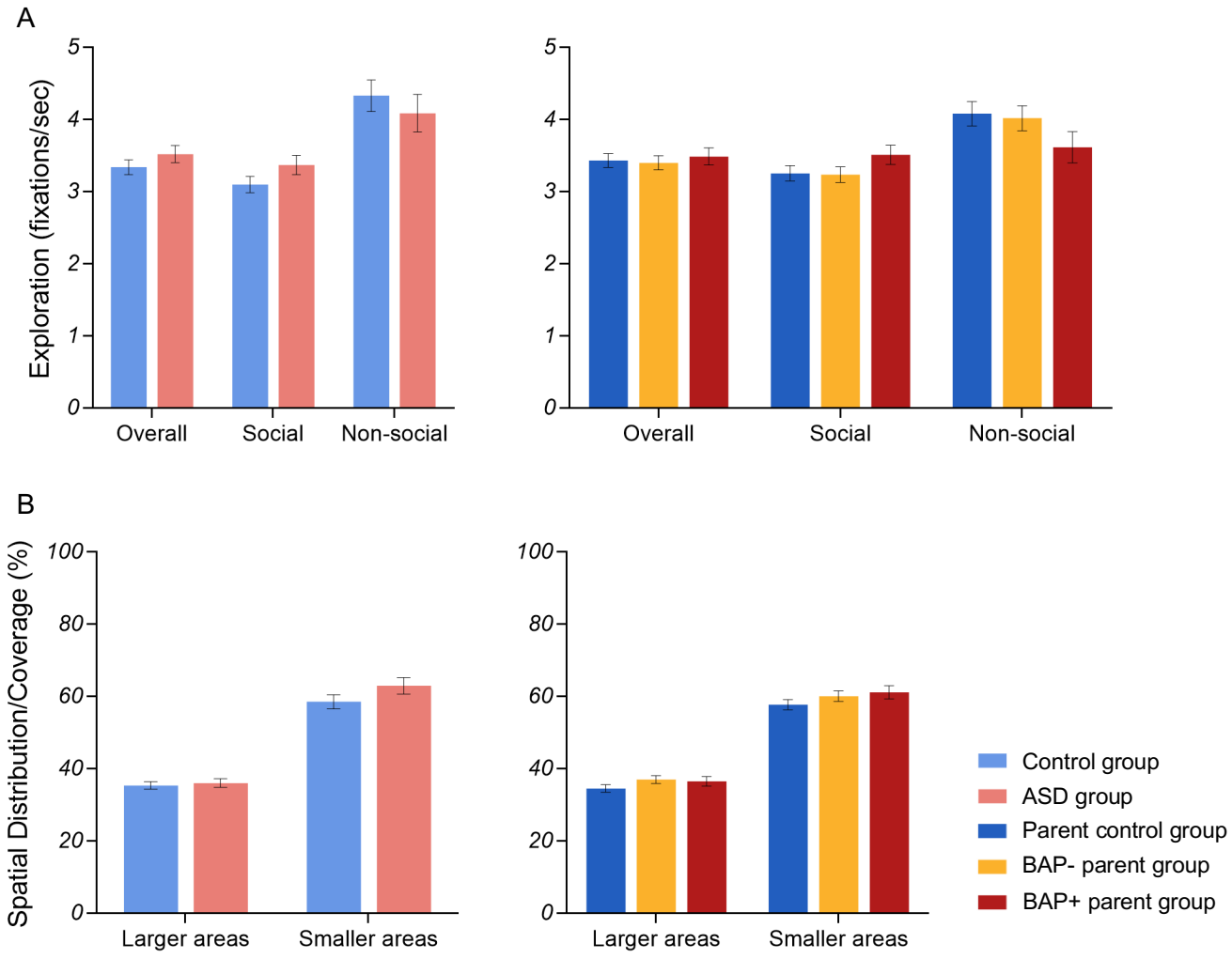

Figure 2.8. *Distribution analyses depicting both A) Coverage exploration (overall) and exploration AOI (social and non-social) and B) spatial distribution/coverage across larger (5 x 4) and smaller (10 x 8) boxes.*

(11) Spatial distribution/coverage:

Probands. There were no significant differences between the ASD and control groups in the percentage of unique areas explored during the matrix for larger ($F_{(1,54)} = .17$, $p = .686$, partial $\eta^2 = .003$) or smaller ($F_{(1,54)} = 2.14$, $p = .149$, partial $\eta^2 = .038$) "boxes".

Parents. Similarly, parents showed comparable area coverage across the larger ($F_{(1,98)} = 2.96$, $p = .088$, partial $\eta^2 = .029$) and smaller ($F_{(1,98)} = 2.39$, $p = .126$, partial $\eta^2 = .024$) grid matrices.

BAP. There were also no differences between BAP+, BAP, and parent control groups in the percentage of fixations covering the scene when the matrix was comprised of large ($F_{(2,97)} = 1.52$, $p = .225$, partial $\eta^2 = .030$) or small ($F_{(2,97)} = 1.29$, $p = .281$, partial $\eta^2 = .026$) "boxes".

Discussion

This study applied a suite of eye-tracking analyses to demonstrate a range of unique methods to assess visual attentional patterns in ASD and the broad autism phenotype (BAP). Specifically, this study examined social and non-social visual attention, as well as general patterns of fixation dispersion across a complex social-emotional scene during a narrative task. In sum, analytical methods examining fixations over the course of the stimulus presentation and repeat perseverative fixations were most robust in differentiating ASD and the BAP from controls, where they evidenced increased non-social or decreased social visual perseveration and decreased social attention over time. As such, these eye-tracking patterns may reflect genetic liability to ASD. Findings additionally highlight the importance of applying unique eye-tracking

methods in revealing nuanced differences of visual attention potentially associated with subclinical traits of a disorder.

Overall gaze variables (i.e., percentage of fixation duration and percentage of fixations) were re-produced from prior work (M. Lee et al., 2019) for purposes of comparison against the unique methods of eye-tracking analyses presented here. Findings revealed that parents with BAP traits spent more time generally fixating on non-social information compared to both parents without BAP features and parent controls. Individuals with ASD in prior work showed similar trending patterns (M. Lee et al., 2019). Unique to the present study, fixations towards social information changed over the course of the task, wherein ASD and BAP+ groups showed unique fixation patterns from controls. Parents with the BAP shifted away earlier from social information, showing decreased social attention over time compared to parents without the BAP and parent controls. While this overall pattern was not significant in individuals with ASD relative to controls, an examination of the data revealed similar fixation patterns over the course of the stimulus presentation in ASD and the BAP. Importantly, divergence analyses demonstrated that individuals with ASD showed significantly reduced social attention towards the middle of the stimulus presentation compared to controls, while BAP+ parents showed a later divergence from parent controls occurring towards the second half, and towards the end of the stimulus presentation compared to both parent controls and BAP- parents. It therefore appears critical to examine timing effects in studies of visual perception and attention, particularly given prior work evidencing delayed global (i.e., Gestalt or integrative) processing in non-social tasks in ASD (Van der Hallen et al., 2015) and atypicalities in the underlying neural correlates indexing face perception in later time windows (J. McPartland, Dawson, Webb, Panagiotides, &

Carver, 2004; J. C. McPartland et al., 2011). It may further suggest that attending towards social information for a prolonged period, may result in information overload (e.g., see review O'Connor & Kirk, 2008). Finally, results highlight how percentage gaze variables may obscure shifting patterns of attentional engagement documented here. As such, an examination of fixations over the course of a stimulus presentation and divergence over specific time bins becomes an important step in further disentangling the nuanced and dynamic nature of gaze inherent to human behavior among these populations.

Prior work (M. Lee et al., 2019) concluded that increased attention allocation towards non-social information in the TAT scene utilized in this present study may reflect greater cognitive effort required to support narrative production (given the nature of the task); however, this pattern of visual attention did not improve narrative quality suggesting that groups capitalized on different sources of information to inform their narratives. As such, increased attention towards non-social information over time, may suggest that *shifting* attention towards non-salient aspects of a scene may be advantageous in informing narratives. It's possible, therefore, that an examination of the second half of the scene, where individuals with ASD and ASD parents have already disengaged from social stimuli as shown in the present study, may align more consistently with prior work (Chawarska et al., 2012) that showed relationships between increased attention to non-salient information and greater clinical-behavioral impairments. For example, individuals with ASD have been observed to demonstrate reduced attention towards the eye region of the face and more attention towards the mouth (Klin et al., 2002b) and, during natural scenes in this same study, increased fixations towards non-social information was associated with poorer social adjustment and increased ASD symptom severity

(Klin et al., 2002b), complementing findings from a later study (Shic et al., 2011) that showed relationships between elevated fixations directed towards the background of a scene that related to increased ASD symptom severity. As such, future studies are encouraged to employ a step-wise method of analyses that first includes an examination of fixations over the course of a task via GCA, followed by an application of divergence time bin analyses, followed by an assessment of traditional and unique gaze analytical tools applied in the present study during critical time windows showing divergent patterns only. Together, that individuals with ASD and the BAP showed decreased fixations directed towards social information over time, suggests that this looking pattern may be particularly sensitive in reflecting ASD genetic vulnerability.

Other eye-tracking indices beyond traditional fixation duration and proportion of fixations were additionally examined, with perseverative fixations (i.e., successive fixations occurring on the same AOI) revealing differences in both ASD and the BAP from controls. Specifically, individuals with ASD showed elevated rates of perseverative fixations towards non-social information and parents with the BAP showed reduced perseverations towards social AOIs. It may be that perseverative fixations reflect rigid tendencies, or a tendency to visually get "stuck" on certain visual information (Hughes & Russell, 1993). Prior work has documented such patterns of perseveration reflected in individuals with ASD or the BAP during eye-tracking tasks involving non-social, illusory shapes (Nayar, Winston, Stevens, & Losh, in prep), social and non-social images (Sasson et al., 2008; Swanson, Serlin, & Siller, 2013), complex scenes (Au-Yeung, Benson, Castelhano, & Rayner, 2011), and language processing (Nayar et al., 2018). Such perseverative tendencies are manifested behaviorally in ASD and the BAP as well. For example, by definition, individuals with ASD exhibit restricted and repetitive behaviors (RRBs),

which include showing an insistence on sameness or increased rigidity in schedules or the environment, as well as repetitive sensorimotor behaviors (Cuccaro, Shao, Grubber, Slifer, Wolpert, Donnelly, Abramson, Ravan, Wright, & DeLong, 2003; K. S. L. Lam, Bodfish, & Piven, 2008; Richler, Bishop, Kleinke, & Lord, 2007a). In the BAP, patterns of perseveration and elevated rigidity tendencies have been documented in every-day life using both self-report questionnaires and semi-structured interviews (Losh et al., 2011; Losh et al., 2009; Losh et al., 2008; Losh et al., 2012; Losh & Piven, 2007; Piven, Palmer, Landa, et al., 1997; Piven et al., 1994). Although research has shown inconsistent relationships between gaze variables and clinical-behavioral features (Chawarska et al., 2012; Klin et al., 2002b; M. Lee et al., 2019; Shic et al., 2011), such patterns of refixations (i.e., perseverative or regressive fixations) have been shown to relate to both lower-order motoric RRBs and social communication in ASD (Nayar et al., 2018; Sasson et al., 2008) and the BAP in parents (Nayar et al., 2018). In a study examining gaze-language coordination (Nayar et al., 2018), authors additionally identified specific associations emerging between refixations in parents with the BAP and elevated rates of RRBs in their children. Findings of atypical perseverative visual attention documented in ASD and the BAP in the present study suggests that perseverative fixations or "sticky" visual attention may help to inform patterns of inheritance of ASD-related candidate endophenotypes. It additionally highlights the utility of examining eye-tracking data using methods beyond traditional fixation and duration eye-tracking variables.

Finally, it is conceivable that increased perseverative fixations towards non-social information in ASD and decreased preservative fixations towards social information may stem from differences in local (i.e., detailed) and global (i.e., integrative) visual processing in ASD

more broadly (Van der Hallen et al., 2015; Van Eylen et al., 2018). Individuals with ASD have been shown to demonstrate heightened local perceptual abilities (i.e., the enhanced perceptual functioning theory) which may result in a reduction in global perceptual abilities (i.e., weak central coherence theory), suggesting that they have difficulty shifting attention from local to a global level (Plaisted, Swettenham, & Rees, 1999; Rinehart, Bradshaw, Moss, Brereton, & Tonge, 2000). Enhanced local perceptual abilities also may explain the tendency for individuals with ASD to more often focus on or get distracted by insignificant, non-salient details in their environment, which has been documented using both eye tracking (Chawarska et al., 2012; M. Lee et al., 2019) as well as through autobiographical accounts (e.g., Grandin, 1995). As such, it is possible that the findings documented in the present study contribute to both the social deficit and weak central coherence/enhanced perceptual functioning theories of ASD, which further necessitates studies examining the links between these theories.

Despite there being significant differences emerging in perseverative fixations, there were few to no differences between proband and parent groups when applying other eye-tracking analytical techniques. Specifically, first fixation AOI or duration did not differ between groups. This was somewhat surprising particularly in light of social orientation atypicalities evidenced in ASD (Franchini et al., 2017; Unruh et al., 2016). It is possible that the demands of the task (i.e., providing a narrative after viewing the picture) influenced visual attention patterns versus other methods such as having participants engage in a passive viewing task in which they may explore the image as they please (Harrop et al., 2018; Sasson et al., 2008). Moreover, given that prior work has shown a lack of social orientation differences in higher functioning individuals with ASD (e.g., Fischer, Koldewyn, Jiang, & Kanwisher, 2014), the greater cognitive ability of the

sample included in the present study (i.e., verbal IQ > 80) may have further contributed to the null findings. First fixation methods may thus be more appropriate during infancy when social orientation comes online, applied to individuals who may have lower IQ, task methods involving passive viewing, and/or more dynamic stimuli.

Similarly, though lack of differences was surprising in exploration (i.e., number of fixations per second), transition, or spatial distribution/fixation coverage analyses, prior work has documented differences in ASD particularly during a face processing task (Shic, Chawarska, et al., 2008a). As such, it may be that the concurrent narrative task demands necessitated both individuals with ASD and controls to explore the complex scene generously and comparably to deduce information to help inform their narratives; this stands in contrast to stimuli depicting motionless faces given their reduced "clutter" and visual complexity. Indeed, there is strong evidence in ASD demonstrating that patterns of fixations vary and depend highly on the context (Chawarska et al., 2012). As such, use of fixation transitions, coverage, and exploration may be applied to future work examining visual attentional differences in the BAP during a face processing task, particularly given distinct face processing emerging in parents that have also been linked to underlying neural correlates (Yucel et al., 2015).

Finally, lack of findings between parent and BAP groups across several variables assessed here was not surprising given that parents of individuals with ASD do not have clinical impairments related to ASD. It was therefore not expected that atypicalities in social attentional patterns among unaffected relatives emerge as robustly as in ASD. This raises important considerations about the underlying mechanisms of the BAP—while social attentional patterns may be a contributing factor to the social atypicalities observed in ASD, this linkage may not

always be the case for the BAP. Future work should aim to delineate these specific indices of BAP more directly in the context of eye tracking. Nevertheless, findings from this study further our understanding of underlying mechanisms contributing to the BAP more broadly.

Taken together, this study highlights the utility of GCA analyses to examine fixations over the course of a task and its application to studies of visual social attention in ASD and the BAP. This type of analyses provides a more nuanced examination of looking patterns over time, which better captures the dynamic aspect of gaze that typically occurs in natural settings; in contrast, average dwell time and proportion of fixation variables assumes a uniform or stagnant method of exploration, and tends to attenuate potential differences in looking patterns. Additionally, perseverations may be specifically tied to greater ASD risk, given their repeated documentation of atypicalities in ASD and the BAP. Despite other variables (i.e., first fixation AOI, first fixation duration, exploration AOI, coverage exploration, transition entropy analyses, spatial distribution/coverage analysis, and regressions) yielding no differences among groups, these variables may be applied to future studies of eye tracking in general, as they are thought to effectively reveal different aspects of underlying cognition (R. W. Booth & Weger, 2013; Eckstein et al., 2017; Hughes & Russell, 1993; Luna et al., 2008; Perea & Carreiras, 2003; Rayner, 1998; Rayner et al., 2010; Zagermann et al., 2018). To the author's knowledge, this is the first study that provides an overview of 11 different types of eye-tracking analytical methods and their application to an ASD and family study framework. Although, limitations include having a relatively small sample size of individuals with ASD and controls, likely impacting the power to detect differences using nuanced eye-tracking variables, as well as their application to only one context (i.e., a complex scene depicting both social and non-social information). As

such, future studies are warranted to further examine how these unique eye-tracking methods may be applied to studies of the BAP across stimuli varying in context. It is also important to acknowledge that the 11 methodological tools documented here, while applicable to research in ASD and subclinical features related to ASD, they only represent a subset of a large number of analytic measures that can be applied to eye-tracking studies (e.g., see Holmqvist et al., 2011). In sum, given the objective and measurable nature of the rigorous eye-tracking variables documented here, the present study has the potential to serve as a template for future eye-tracking studies examining visual attention across any population.

CHAPTER 3: Visual perception and central coherence in ASD and parents: A family genetic eye-tracking study

Abstract:

Background: Individuals with ASD often demonstrate a local visual processing bias, with conflicting evidence showing concurrent impaired global processing. Importantly, atypicalities in global visual processing have been associated with increased ASD symptom severity, shedding light into potential biological mechanisms contributing to the ASD phenotype. Visual attentional differences have also been documented more subtly among parents of individuals with ASD. However, prior studies involving parents have not assessed local/global visual processing explicitly, particularly using objective methods of measurement beyond accuracy and reaction time alone. As such, the extent to which visual perception may constitute a potentially heritable endophenotype linked to ASD-related features, remains unknown.

Methods: Participants included a maximum of 32 individuals with ASD and 30 controls, as well as 56 parents of individuals with ASD and 43 parent controls. Participants completed two interactive tasks that tap local and global visual processing, administered on an eye tracker. To examine bottom-up visual (local and global) processing, performance (i.e., accuracy and reaction time) and a suite of eye-tracking variables—i.e., exploration (number of fixations per second), vacillation (percentage of fixations shifting from the target match to the non-target match), and three composite gaze scores reflecting local/global perception across tasks were calculated. A series of linear mixed effects models were applied to proband (i.e., ASD versus control) and

parent (i.e., ASD parent and control parent) groups to assess group differences. Within-family associations of local/global perception were examined separately for ASD and control families and correlations were conducted between local/global processing and clinical and subclinical traits related to ASD.

Results: Significant differences emerged for performance (i.e., accuracy and/or reaction time) indices during more complex tasks in proband and parent groups. Eye-tracking results revealed evidence of reduced global versus local visual processing in ASD and ASD parent groups. Findings specifically revealed heightened local processing (i.e., elevated rates of exploration and vacillations), in addition to reduced global perception in individuals with ASD. In contrast, ASD Parents, demonstrated a diminished bias towards global stimuli, without indications of heightened local processing (i.e., no differences in exploration and vacillation), compared to the parent control group. Within family similarities of processing styles emerged primarily for ASD parent-child pairs, but not for unrelated pairs or control parent-child pairs. Finally, heightened local processing related to elevated rates of restricted and repetitive behaviors in individuals with ASD; whereas unexpected relationships with better pragmatic language abilities was observed in both ASD proband and parent groups.

Conclusions: Findings demonstrated robust local/global visual processing differences using eye tracking in individuals with ASD versus controls, with subtle, and nuanced differences emerging among parent groups. Differences observed in the present study might point to underlying neurobiological differences in visual perception. Within-family associations suggests that visual

processing styles uniquely co-segregate in ASD families, indicating potential heritability. Associations with clinical-behavioral features related to ASD suggest that local/global processing styles may differentially impact broader traits related to ASD. Together, eye-tracking findings suggest that visual processing styles may be heritable, genetically meaningful features of the broader autism spectrum, thereby underscoring their contributions to further understanding the broad autism phenotype (i.e., sub-clinical features mirroring the core symptoms of ASD present in unaffected first-degree relatives) and highlighting their utility as a candidate endophenotype.

Introduction

An essential component of visual perception is *global processing,* or seeing the gist, which involves the integration of local segments of a scene to create an integrated whole in a rapid and automatic fashion (Kimchi, 1992; Navon, 1983). This perceptual process is the typical and default perceptual strategy used by adults (Navon, 1977) and undergoes a protracted developmental trajectory from local to global processing, with adult-like global perceptual strategies emerging after age 7 years (Nayar et al., 2015). In contrast, *local perception* is the selective attention to parts of a scene (Kovacs, 1996; Navon, 1977), usually characteristic of young children's perceptual styles, and generally slower than global processing (Freeseman et al., 1993; Kimchi, 1992; Navon, 1977; Nayar et al., 2015). These processes in tandem support the fluid interpretation of our environment, and social worlds in particular. Impairments in seeing the "big picture" (i.e., weak central coherence theory) may relate to social skills, verbal and nonverbal communication, and cognition more generally (Behrmann et al., 2006; Burnette et al., 2005; Happe, 1999; Jarrold et al., 2000; Jolliffe & Baron-Cohen, 2000; Klin et al., 2002b; Van Eylen et al., 2018). Differences in visual perceptual styles, including a local perceptual bias (i.e., enhanced perceptual functioning theory), are thought to underlie some aspects of the social-communicative difficulties observed in autism spectrum disorder (ASD; a neurodevelopmental disorder characterized by deficits in social communication and the presence of repetitive behaviors or circumscribed interests) (APA, 2013). For example, local perception may be reflected in face processing, whereby an individual may fixate only on one part of the face, making it challenging to interpret facial expressions (Van der Hallen et al., 2015; Van Eylen et

al., 2018). Similarly, findings suggest that intact global processing abilities relate to more positive outcomes in those with ASD (Fitch et al., 2015).

There exists conflicting findings of local/global perceptual abilities in ASD wherein there exists no differences from controls or that they show superior local processing and/or deficits in global processing relative to controls (Frith, 1989; F. Happe, 1996; Koldewyn, Jiang, Weigelt, & Kanwisher, 2013; Milne & Scope, 2008; Mottron, Burack, Iarocci, Belleville, & Enns, 2003; Mottron, Burack, Stauder, & Robaey, 1999; Plaisted et al., 1999; Rinehart et al., 2000; Ropar & Mitchell, 1999, 2001) and first-degree relatives (Bolte & Poustka, 2006; Briskman et al., 2001; Losh et al., 2009; Neufeld et al., 2020; Van Eylen et al., 2017). These studies primarily used performance-based outcome measures (i.e., accuracy and reaction time measures alone), and may show conflicting findings as a result of methodological differences across studies (e.g., guided instructions) (see meta-analysis Van der Hallen et al., 2015). A study combining performance *and* eye-tracking methodologies to assay global perception in ASD (Nayar et al., 2017), documented reduced global processing abilities in the absence of heightened local perception in ASD compared to controls. While inconsistent with the majority of the literature that documents heightened local processing, these findings were captured primarily using eye tracking, thus illuminating clear strategy differences that may have been missed from performance measures alone, and therefore highlighting the utility of objective measures such as eye tracking to study visual perception.

Evidence also suggests that eye-movement patterns (including saccade trajectories and information that trapped attention) are heritable in the general population (Constantino et al., 2017) and across psychiatric disorders (Ettinger et al., 2004), implying that gaze patterns may

reflect underlying genetics and neurobiological mechanisms contributing to a disorder and constitute endophenotypes (i.e., heritable characteristics more proximal to the genetic causes of a disorder) (Gottesman & Gould, 2003). As such, studies of gaze and eye movements in families affected by ASD may potentially inform the underlying mechanisms related to ASD symptoms and underlying neurobiology. For instance, eye tracking has the potential to reveal nuanced information of underlying strategies and cognition (Awh et al., 2006; Grosbras et al., 2005; Just & Carpenter, 1975; Luna et al., 2008; Theeuwes et al., 2009; Thomas & Lleras, 2007; Van der Stigchel et al., 2006; Yarbus, 1967), that can be mapped onto underlying biology (Eckstein et al., 2017). Specifically, differences in local/global visual processing identified via eye tracking may indirectly inform an understanding of the neurobiological mechanisms involved in such processes, particularly within the visual cortex (Altmann, Bulthoff, & Kourtzi, 2003; T. S. Altschuler et al., 2014; Altschuler et al., 2012; Doniger, Foxe, Murray, Higgins, & Javitt, 2002; Doniger et al., 2000; Doniger, Foxe, et al., 2001; Fink et al., 1997; Foxe et al., 2005; Stroganova, Orekhova, et al., 2007; Stroganova et al., 2012), which may interact with higher-order biological processes tapping social attention and social communication (Keehn et al., 2020). Gaze and eye movement may therefore serve as particularly good candidate endophenotypes, given their known heritability and association with ASD (Constantino et al., 2017; Neufeld et al., 2020); however, few studies have explored local and global visual perception using eye tracking in unaffected family members who are at increased genetic liability to ASD.

Family members may demonstrate a constellation of subclinical features believed to index genetic liability to ASD (i.e., the broad autism phenotype, BAP) (Losh et al., 2009; Losh et al., 2008; Losh & Piven, 2007). Specifically, a subset of relatives of individuals with ASD

demonstrate personality features (e.g., aloof or rigid personality traits, pragmatic language differences) that mirror the social and repetitive behavior domains of impairment in ASD, as well as subtle differences in global processing, social cognition, and reading (Adolphs et al., 2008; Bolte & Poustka, 2006; Briskman et al., 2001; Chouinard, Unwin, Landry, & Sperandio, 2016; Constantino et al., 2017; Cribb et al., 2016; Hogan-Brown et al., 2014; M. Lee et al., 2019; Mosconi et al., 2010; Nayar et al., 2018; Neufeld et al., 2020), which have been observed in family members of individuals with ASD. Eye movements have also been found to differ among parents of individuals with ASD compared to controls across a range of tasks tapping social attention (Groen et al., 2012; M. Lee et al., 2019) and language processing (Nayar et al., 2018). In particular, parents presenting with BAP features showed reduced language automaticity that coupled atypical, perseverative (i.e., getting "stuck") and regressive (i.e., moving backwards) eye fixations, which related to patterns of restricted and repetitive behaviors (RRBs) in their children with ASD (Nayar et al., 2018). These studies provide intriguing evidence that certain features of a stimulus may "trap" the attention of individuals with ASD and the BAP and which may reflect a local perceptual style. They further add to our understanding of potential underlying mechanisms that contribute to observed sub-clinical features related to the BAP.

Prior studies have revealed some differences in local and global processing among relatives of individuals with ASD (Bolte & Poustka, 2006; Briskman et al., 2001; Neufeld et al., 2020; Van Eylen et al., 2017), mirroring the visual processing styles identified among those with ASD (Van der Hallen et al., 2015; Van Eylen et al., 2018). Specifically, heightened local perception has been documented among parents of individuals with ASD using the Block Design task (a task that involves piecing together a set of blocks to make a specific pattern) (Bolte &

Poustka, 2006; Happe, Briskman, & Frith, 2001); however, this finding was not replicated in a larger sample of parents (Losh et al., 2009), perhaps due to methodological differences (e.g., segmented versus unsegmented block designs), differences in performance between fathers versus mothers (Happe et al., 2001), or variability in processing styles among parents. Van Eylen et al. (2017) found that parents of individuals with ASD paid greater attention to detail in daily life according to a self-report questionnaire. The authors did not find differences in performance-based indices in experimental tasks of local and global processing, perhaps reflecting the limitations of accuracy and reaction time measures to reveal differences within a group exhibiting sub-clinical traits. Importantly, a recent twin study of individuals with ASD revealed striking similarities among monozygotic twins in performance measures during tasks tapping local perception that also related to ASD severity (Neufeld et al., 2020), suggesting that visual perceptual styles may reflect underlying genetics contributing to ASD symptomatology. Such differences in local and global visual perception have even been found to vary as a function of BAP-related traits among the *typical* population (Chouinard et al., 2016; Cribb et al., 2016; DiCriscio, Hu, & Troiani, 2019; Hayward, Fenerci, & Ristic, 2018), revealing a potentially powerful ASD-related endophenotype.

The present study builds on existing performance-based (i.e., accuracy, reaction time) studies of local and global processing by providing detailed characterization of eye movement, in addition to traditional performance-based measures, in individuals with ASD and their parents. This study utilized two interactive match-to-sample tasks, whereby participants were presented with an image for a short amount of time, followed by two images -- one that matched the sample, and one that did not match the sample -- requiring the participant to select the match (see

Methods for more details). Studies of central coherence have shown atypical processing in individuals with ASD, though findings have been inconsistent (Frith, 1989; F. Happe, 1996; Koldewyn et al., 2013; Milne & Scope, 2008; Mottron et al., 2003; Mottron et al., 1999; Plaisted et al., 1999; Rinehart et al., 2000; Ropar & Mitchell, 1999, 2001), mainly due to methodological differences in both the type of stimuli and administration methods (e.g., drawing, guided instructions, match-to-sample tasks) (see meta-analysis, Van der Hallen et al., 2015). A large body of research has used the Navon stimuli to study global precedence effects and local and global processing *interference* effects (Koldewyn et al., 2013; Mottron et al., 2003; Navon, 1977; Plaisted et al., 1999), embedded figures tasks (e.g., Jolliffe & Baron-Cohen, 2000; Ropar & Mitchell, 2001) and block designs (e.g., Briskman et al., 2001) to study general local/global processing based on behavioral measures, and faces to assess configural processing (e.g., Behrmann et al., 2006). Face perception represents a specific level of expertise (Happe & Frith, 2006) that might not be suited for generalization to the perception of objects in our environment. Additionally, Block Design, in addition to using visuospatial skills, also requires the ability for individuals to manually manipulate materials. The required integration of fine motor skills and visual perception to complete block design tasks therefore does not isolate perceptual abilities like object and face stimuli do. Finally, other stimuli, like the Navon, while extensively used in the literature, do not necessarily have a "correct" response and inherently imply competition between local and global processing such that task-irrelevant level of visual processing is present and conflicts with the primary level of global visual processing (Happe & Frith, 2006; Van der Hallen et al., 2015). Moreover, they require *selective attention* to the local or global levels of the stimulus, tapping into both attentional and perceptual mechanisms. As such, stimuli utilized in

the present study included the use of Kanizsa Illusory Contours (Kanizsa, 1976) or KICs *(Fig. 3.1A*), in which strategically placed "pacman" elements induce an illusory shape; typically, perceivers using a global strategy immediately experience the "pop out" effect and automatically extract the illusion; however, if using a local strategy, these stimuli can be perceived as unassociated "pacman" elements. KICs have been used extensively in the neuropsychological literature to study the development of global form processing in typical development (e.g., T. S. Altschuler et al., 2014; Bulf, Valenza, & Simion, 2009; Cox et al., 2013; Harris et al., 2011), as well as in psychiatric (e.g., Keane, Joseph, & Silverstein, 2014) and ASD (Baruth et al., 2010; Stroganova, Nygren, et al., 2007; Stroganova, Orekhova, et al., 2007; Stroganova et al., 2012) populations. They provide a fruitful model for investigating local and global perception and contextual integration since they are easily quantifiable, affording correct responses (i.e., they elicit specific shapes like a square). Moreover, there are no interference effects from crowding in the classic KIC stimuli. Many studies have also specifically studied the neurological underpinnings of local and global perception when viewing illusory contours: lower, early visual areas are suggested to be involved in contour completion and may be used in focusing on the individual elements of an illusory contour (T. S. Lee & Nguyen, 2001; Maertens & Pollmann, 2005); while higher order visual areas (e.g., lateral occipital complex) have been associated with higher level perceptual skills such as object representation and completion, and may be involved in integrating the local pacman elements together to form the coherent whole (Harris et al., 2011; Ringach & Shapley, 1996; Stanley & Rubin, 2003). Feed-forward and feed-backward mechanisms also appear to be involved in KIC perception between higher and lower visual areas (M. M. Murray et al., 2002; Scholte, Jolij, Fahrenfort, & Lamme, 2008; Wokke, Vandenbroucke,

Scholte, & Lamme, 2013). This suggests that local and global perceptual strategies involved in KIC perception may provide valuable insights into the neural mechanisms involved in their perception in individuals with ASD and their parents. Given their extensive use in the literature to examine local and global processing and interference effects, the Navon hierarchical figure (Navon, 1977) was additionally used in a match-to-sample paradigm, similarly requiring participants to select the Navon that best matched the sample. Because prior work has been limited in the capacity to document *strategies* of performance during local/global tasks, typically focusing only on reaction time and accuracy performance-based measures (Van der Hallen et al., 2015), this study incorporated a suite of eye-tracking variables to document strategies underlying behavioral performance, particularly given their prior success in KIC paradigms (Nayar et al., 2015; Nayar et al., 2017) and in tapping subtle differences as a manifestation of subclinical BAP features in parents (M. Lee et al., 2019; Nayar et al., 2018).

Eye-tracking variables utilized in this study tap either local or global processing, and unveil underlying strategies for task completion. For instance, the number of *vacillations* between two stimuli can point to levels of uncertainty and readiness to appreciate the global form, with greater vacillations indicating a higher level of uncertainty and reduced appreciation for the global percept, which are characteristic of younger children (Nayar et al., 2015). Similarly, levels of *exploration*, or the number of fixations occurring per second, generally indicates attentional capacity and cognitive load (Zagermann et al., 2018), with elevated values reflecting higher levels of disengagement or serial/local processing strategies. In contrast, the location of the first fixation is thought to index the utilization of peripheral visual information, which is associated with global or rapid and automatic visual information processing and

generally reflects visual information preference (Kimchi, 1992). Relatedly, increased levels of fixations or time spent fixating on the target (i.e., the stimulus that matches the sample previously presented) has been shown to index greater global processing that has also been reflected in unique patterns of neural processing during local/global tasks with target and non-target stimuli (Baruth et al., 2010; Fink et al., 1997; Heinze, Hinrichs, Scholz, Burchert, & Mangun, 1998). Finally, gaze directed towards different components of the KIC stimuli reflect unique perceptual processes. For instance, there is evidence of a "pop out" effect in appreciating the global form (i.e., the illusory shape), which prior work has demonstrated correspond to visual attention directed towards the "center" of the KIC indicating greater global perception, in contrast to looking towards the individual pacman elements, which reflects a greater local processing strategy (Guttman & Kellman, 2004; Ringach & Shapley, 1996). Together, eye-tracking variables applied to the interactive tasks in the present study provided unique information about performance strategy beyond performance-based measures alone.

This study aimed to 1) explore group differences in local/global processing and identify local/global processing profiles among groups, 2) examine parent-child associations in global/local processing profiles to explore familiality of traits, and 3) assess the relationships of local/global profiles to clinical and subclinical traits of ASD. Studying such traits in families may provide a more powerful approach for unveiling the roots of ASD clinical features than studying the full clinical phenotype. It was therefore hypothesized that individuals with ASD will demonstrate a style that is less reliant on global processing compared to controls (i.e., demonstrate fewer fixations and time spent attending towards the centers of the KICs, and the target stimuli, as well as elevated rates of exploration and vacillations between the two options),

with similar, but less pronounced, trends observed in parents. Specifically, it was predicted that there will be no evidence of group differences emerging in performance-based measures of accuracy and reaction time between parents, but that strategy-based measures of eye tracking, though exploratory, may capture subtle differences between parent groups. Similarly, it was anticipated that local/global processing would relate to both ASD and BAP features including core language and restricted and repetitive behaviors in ASD and pragmatic language and rigid personality traits in parents. In order to examine whether local/global processing abilities relates to social cognition, particularly given that prior work has demonstrated some, albeit inconsistent, ties to social cognition (Burnette et al., 2005; Happé, 2000; Martin & McDonald, 2003; Pellicano, Maybery, Durkin, & Maley, 2006) and because of documented social cognitive deficits in ASD (Baron-Cohen, Wheelwright, & Jolliffe, 1997) and subtle differences in parents (Baron-Cohen & Hammer, 1997; Losh & Piven, 2007), it was predicted that a local processing bias or weakness in global processing would relate to weaknesses in social cognition in ASD. Though exploratory, similar relationships may emerge in parents. Additionally, there exists a debate in the literature regarding the independent or dependent role of executive functioning in local/global processing (R. Booth, Charlton, Hughes, & Happe, 2003; Happe & Frith, 2006; Van Eylen et al., 2017; Van Eylen et al., 2018), which argues that local and global perception is an executive (versus a perceptual) impairment. On the other hand, there is evidence to suggest that they are inherently separate entities (Bolte, Holtmann, Poustka, Scheurich, & Schmidt, 2007; Rinehart et al., 2000; Van Eylen et al., 2017). Given that KIC taps perceptual processes, particularly with distinct underlying neural correlates along the occipito-parietal visual regions of the brain, we do not expect relationships between executive functioning and local/global

processing in any group. Finally, parent-child correlations will be documented in both ASD and control families, with stronger familial effects expected to emerge in ASD families. Finally, parent-child correlations will be documented in both ASD and control families, with stronger familial effects expected to emerge in ASD families.

Methods

Participants.

Across tasks, participants included 32 individuals with ASD and 30 controls. The ASD parent and parent control groups were comprised of 57 and 43 individuals, respectively. Parents were included in the ASD parent group if they had at least one child with idiopathic ASD. There were 16 dyadic pairs (i.e., parent-child) in ASD families and 21 control dyads. ASD and control families were recruited through prior and ongoing studies. Recruitment efforts additionally included advertisements to ASD clinics, advocacy organizations and participant registries and word of mouth. Inclusionary criteria for all participants included speaking English as their first language, a minimum full-scale IQ (FSIQ) of 70, age of 8 years or older no uncorrected visual impairment (s) (e.g., strabismus, uncorrected double vision), no history of neurological conditions (e.g., brain injury, seizures), and no known genetic syndrome associated with ASD or major psychiatric disorder (i.e., bipolar, schizophrenia, and related psychotic disorders). Control participants were included if they had no personal or family history of ASD or related genetic disorders (e.g., fragile X syndrome), as well as no family member within their nuclear family with a history of depression or language-related delays. See *Table 3.1* for demographic characteristics of the participant sample. All study procedures were approved by Northwestern

University's Institutional Review Board and written informed consent/assent was obtained for all participants.

***Table 3.1*:** Sample Characteristics

KIC and Navon*	**Control Group**			**ASD Group**			**Group Difference**		
	M	**Range**	**SD**	**M**	**Range**	**SD**	***t***	**df**	***p***
Probands n (M/F)		**30 (18/12)**			**32 (25/7)**		-	-	-
Age (years)	14.75	8.25 - 35.64	6.02	15.97	9.53 - 32.42	4.72	-0.89	60	0.378
FSIQ	116.8	88 - 145	13.6	97.9	73 - 135	16.0	4.98	60	**< .0001**
VIQ	117.2	93 - 142	13.3	98.7	69 - 142	18.6	4.48	60	**< .0001**
PIQ	116.0	79 - 149	16.9	97.8	68 - 136	17.3	4.18	60	**< .0001**
ADOS Total Severity Score^	-	-	-	8.3	5 - 10	1.3	-	-	-
SA Severity Score	-	-	-	8.1	4 - 10	1.4	-	-	-
RRB Severity Score	-	-	-	8.0	1 - 10	1.8	-	-	-
Parents n (M/F)		**43 (11/32)**			**57 (19/38)**		-	-	-
Age (years)	45.40	31.85 - 67.83	9.32	48.29	35.62 - 61.8	6.86	*-1.72*	*74.08*	*0.090*
FSIQ	118.3	83 - 134	11.4	111.7	85 - 136	12.1	2.77	98	**0.007**
VIQ	114.8	84 - 132	10.7	110.4	80 - 131	12.0	1.93	98	0.057
PIQ	116.6	86 - 136	11.2	110.1	79 - 137	12.0	2.76	98	**0.007**

*Sample descriptives include maximum participants across tasks; Age is averaged between KIC and Navon administration dates if different. Bold indicates significance $p < .05$; Italics indicates unequal variance assumed; ^Comparison severity score labels are as follows: 0-2 = “minimal-to-no evidence”, 3-4 = “low”, 5-7 = “moderate”, 8-10 = “high”. ADOS, Autism Diagnostic Observation Scale; FSIQ, Full-Scale IQ; PIQ, Performance IQ; RRB, Restricted and Repetitive Behaviors and Interests; VIQ, Verbal IQ.

Clinical-behavioral Characterization.

Assessment of Cognitive Ability. The Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) or the Wechsler Intelligence Scale for Children—Third Edition (WISC-III) (Wechsler, 1991) was used to assess 2-subject or full-scale (FSIQ), verbal (VIQ), and performance (PIQ) IQ. The ASD group had a significantly lower FSIQ, VIQ, and PIQ than the control group (*p*s<.0001), and the ASD parent group had significantly lower FSIQ and PIQ than their respective controls (*p*s < .01).

Assessment of ASD Symptoms. The Autism Diagnostic Observation Schedule-General or 2nd Edition (ADOS) (Lord et al., 2012) and/or the Autism Diagnostic Interview-Revised (ADI-R) (Lord et al., 1994) were used to confirm a diagnosis of ASD. ADOS calibrated severity scores (total, social affect, and restricted and repetitive behavior) (Gotham, Pickles, & Lord, 2009) were additionally calculated. Moreover, the Social Responsiveness Scale (SRS) (Constantino & Gruber, 2005), and the Repetitive Behavior Scales-Revised (RBS-R) (K. S. Lam & Aman, 2007) questionnaires were obtained to further characterize symptoms of social communication and restricted and repetitive behaviors.

Assessment of the Broad Autism Phenotype in Parent-ASD Group. Personality features associated with the BAP (i.e., sociability, rigidity, and pragmatic language) were assessed among parents of individuals with ASD. Assessments included a semi-structured interview, the Modified Personality Assessment Scale-Revised (MPAS-R) (Piven, Palmer, Landa, et al., 1997), which includes a series of questions specifically designed to tap the subclinical features related to the BAP including aloof, rigid, perfectionistic, and untactful personality traits. Coding of personality features followed methods outlined in prior work, such that raters were assigned

scores ranging from 0 to 2 (trait absent, possibly present, definitely present) on a 5-point Likert scale. The broad autism phenotype questionnaire (BAP-Q) (Hurley, Losh, Parlier, Reznick, & Piven, 2007) was used to further characterize BAP traits in a continuous manner including total scores, aloof and rigid traits, and pragmatic language violations.

Assessment of Pragmatic Language. Pragmatic language was assessed using the Pragmatic Rating Scale (PRS) (R. Landa et al., 1992) (for parents) and Pragmatic Rating Scale-School Age (PRS-SA) (R. Landa, 2011) (for ASD and controls). Raters blind to family diagnosis rated language and speech behaviors that were operationally defined based on a semi-structured conversation about the participant's Life History and a conversation that is incorporated into the ADOS, respectively. The PRS has been repeatedly shown to distinguish relatives of individuals with ASD from controls (R. Landa et al., 1992; Piven et al., 1990; Piven et al., 1994).

Assessment of Social Cognition. The Reading the Mind in the Eyes Test (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001) assesses recognition of complex psychological states by viewing photographs depicting only the eye region of the face, presented with four complex mental state words, in which the participants must select which of the four words best represents the eyes in each photograph. Prior work has demonstrated deficits in ASD (Baron-Cohen et al., 1997), and subtle differences have been reported in parents (Baron-Cohen & Hammer, 1997; Losh & Piven, 2007). Though inconsistent, prior work has additionally indicated relationships between local/global processing and theory of mind abilities in ASD (Burnette et al., 2005; Happé, 2000; Martin & McDonald, 2003; Pellicano et al., 2006).

Assessment of Executive Functioning. Given theories and literature documenting relationships with executive functioning and local/global processing (R. Booth et al., 2003;

Happe & Frith, 2006; Van Eylen et al., 2017; Van Eylen et al., 2018), suggesting that local and global perception is an executive (versus a perceptual) impairment, two executive functioning measures were examined as correlates. The Flanker (Eriksen & Eriksen, 1974) test from the NIH Toolbox (Weintraub et al., 2013) was administered to a subset of ASD parents, individuals with ASD, and controls, as an experimental measure of selective attention and inhibitory control. The BRIEF-parent (Gioia, Isquith, Guy, & Kenworthy, 2000) and BRIEF-Adult (Roth, Lance, Isquith, Fischer, & Giancola, 2013), specifically the Global Executive Composite (GEC) T-score, was used as a measure of overall executive functioning impairments in daily life among groups.

Design and Stimuli.

General Procedures

Participants completed two interactive similarity match-to-sample (i.e., selection of a target image that matches a sample) tasks involving KIC and Navon figures (see, "Kanizsa Illusory Contour Task" and "Navon Hierarchical Figure Task" below) to assess indices of global processing including accuracy, reaction time, and a suite of eye movements variables as outlined below. Tasks were presented on a 17-inch TFT LCD monitor (1,280 x 1,024 resolution) placed 50-60 cm away from the participant. Before each test run, all participants completed a practice run on which 80% accuracy was required to ensure mastery of task instructions. A Tobii T60 eye tracker (Tobii Technology AB, Danderyd, Sweden) was used to track gaze coordinates at a rate of 60 Hz. Prior to task administration, a standard 5-point calibration grid was used, which renders a typical visual angle accuracy of 0.5°. Participants were recalibrated following any large

movements during calibration, and tracking was additionally monitored during the task using the live view and track window options in Tobii Studio. Finally, calibration checks were embedded in the task (e.g., center cross-hair) to ensure tracking accuracy throughout the duration of the task.

Kanizsa Illusory Contour (KIC) task.

KIC Paradigm. The KIC task consisted of three interactive similarity match-to-sample conditions (*Fig. 3.1B*) presented in a fixed order across all participants: first, the practice condition, then the two test conditions (*KIC basic* followed by *KIC noise* (see below)), based on Nayar and colleagues' previous work (Nayar et al., 2015; Nayar et al., 2017). On each trial across the three conditions, one of five non-illusory solid shapes (square, diamond, rectangle, triangle, or trapezoid) appeared for 1 second at the center of the screen, followed by a blank (black) screen for 1 second, after which two simultaneously presented figures appeared—the two figures were non-illusory solid shapes for the practice condition, and KIC figures for the test conditions. All participants were instructed to respond as quickly as possible. Verbal feedback indicating accuracy was only provided during the *KIC practice* condition; in contrast, neutral phrases of encouragement were periodically provided (approximately every 10 trials depending on the participant's level of attention and engagement), such as saying, "keep it going!", "You're moving along nicely!", or "almost there!". Across conditions, every participant was informed when the condition was at the mid-way point (i.e., 12 or 20 trials, respectively). Finally, at the beginning of each condition, participants were briefly reminded of the match-to-sample instructions, without mentioning illusory forms during instructions.

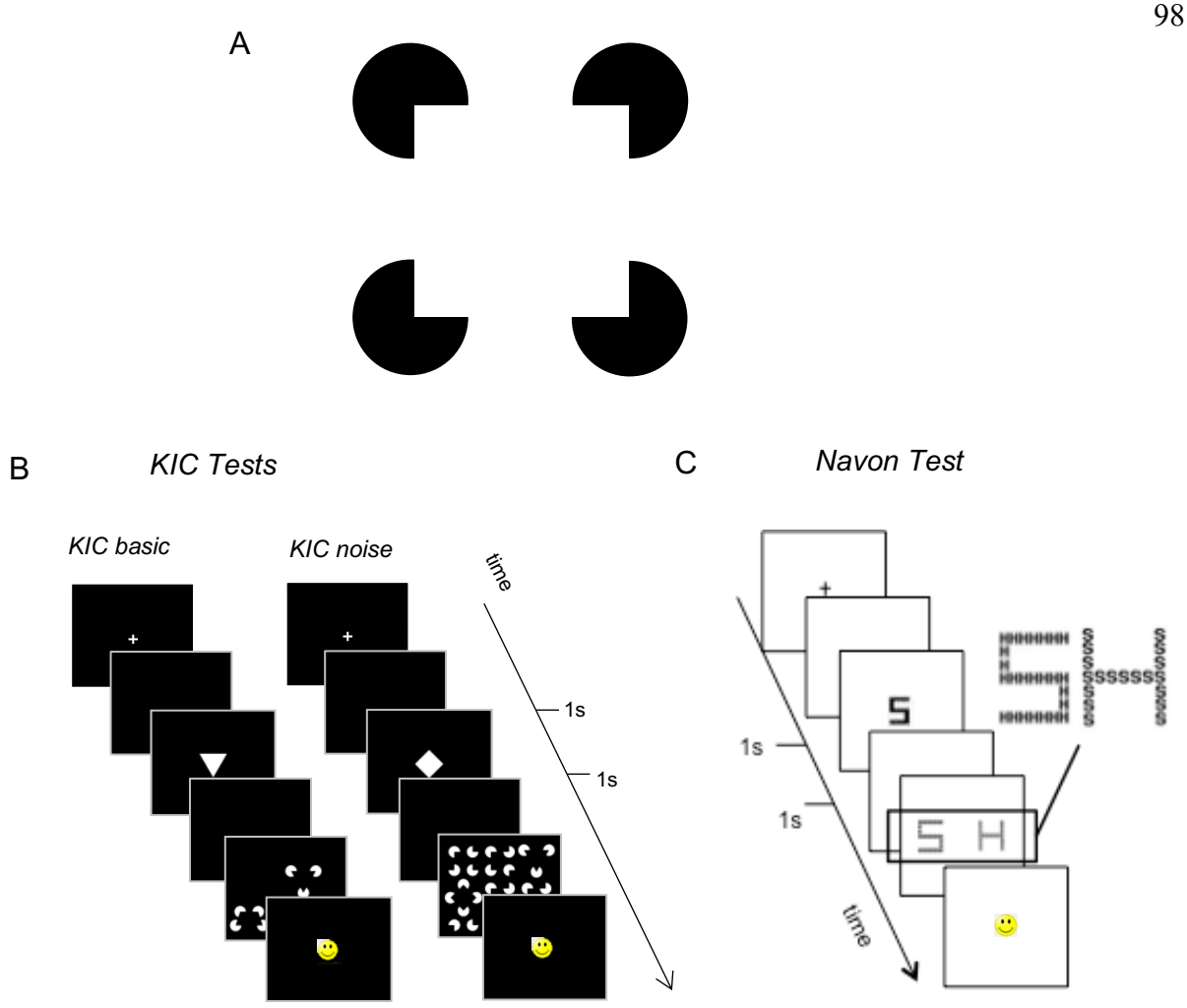

Figure 3.1. *Stimuli presented. a) an example of a Kanizsa Illusory Contour (KIC) with an illusory square percept; b) match-to-sample sequence of test stimuli for the KIC Paradigm (KIC basic and KIC noise, respectively) using KICs; c) match-to-sample sequence of test stimuli for the Navon Paradigm, using hierarchical Navon figures*

KIC Figure Parameters. Support ratio (the relative length of the inducing versus induced contour) of all the KIC figures was set at 60% and based on prior work (Nayar et al., 2015; Nayar et al., 2017). The size of the KIC figures was fixed and consistent with prior work (Nayar et al., 2017)—at a distance of 60cm, the pacman elements' radius was 1.5° and the illusory edge was 5°. As such, the total edge length was 8°. All figures were white on a black background with average luminance for each solid shape set at 180 cd/m^2 and the background at 35 cd/m^2.

KIC Practice Condition. All participants completed a *KIC practice* condition, in which 24 trials of real (non-illusory) shapes were presented in order to prevent potential training effects on the illusory KIC figures. The *KIC practice* condition was administered prior to the test conditions and was administered once mastery (80% accuracy) was achieved, with up to three attempts. During this condition, a smiley face was displayed only after correct responses.

KIC Basic and KIC Noise Test Conditions. Following mastery of the task, two test conditions were administered in a fixed order: 1) a *KIC basic* test condition assessing basic KIC recognition, and 2) a *KIC noise* test condition that assessed KIC recognition in the presence of background "noise" consisting of randomly places pacman elements. This condition therefore generated local interference as a means to assess how task-irrelevant information (i.e., local pacman distractors) may interfere with global processing of the KIC figure (Nayar et al., 2017; Van der Hallen et al., 2015). During both test conditions, participants were required to select one of two KIC figures that matched a previously presented non-illusory sample shape—one KIC figure induced the appearance of the non-illusory sample shape (i.e., "target KIC" or the match), and one that did *not* match the sample (i.e., "distractor KIC"). The target and distractor KIC figures appeared on either the left or the right side of the screen's vertical midline. The KIC figures were further randomized across these two halves, separating the screen into four quadrants—upper and lower left, and upper and lower right quadrants. To further avoid position biases, the target KIC figure was limited to presentation on the same side for four consecutive trials only. While the *KIC basic* condition included only two KIC figures, the *KIC noise* condition presented two KIC figures embedded in a background of "noise". Unlike the *KIC practice* condition, a smiley face was presented following each click response regardless of

accuracy to prevent learning effects. Further, to ensure that participants responded and to encourage engagement, the examiner presented the next trial only after the participant appeared ready (i.e., facing the screen, hand placed on the mouse, not talking). Both test conditions consisted of 40 trials.

Navon Hierarchical Figure (Navon) task.

Navon Paradigm. Similar to the KIC task, the Navon task consisted of two interactive match-to-sample conditions (*Fig. 3.1C*) presented in a fixed order across all participants: 1) a practice condition and 2) the test condition. The format of the match-to-sample paradigm was consistent to the KIC paradigm such that an image appeared at the center of the screen for 1 second, followed by a blank (white) screen for 1 second, followed by two simultaneously presented images. For both conditions, the two figures appeared in fixed positions, appearing on either side of the screen's midline. The target (or match) figure did not repeat on the same side for more than four consecutive trials. Feedback for practice versus test conditions was consistent with that of the KIC Paradigm.

Navon Hierarchical Figure Parameters. The Navon figure is made up of a large letter, composed of smaller different letters. Navon figures were separated into two categories: those that were morphologically *similar* (e.g., F and E) and those that were morphologically *dissimilar* (e.g., O and N) (Lamb & Robertson, 1989; Mottron et al., 1999) (*Table 3.2*). Consistent with prior work (Koldewyn et al., 2013; Mottron et al., 1999), at a distance of 60cm, the large Navon figure was 5° long and 3.5° wide with the size of the smaller letters fixed at .5 x .5°. Letters were black against a white background.

Table 3.2. Navon morphologically similar and dissimilar letters presented in a pseudo-random order (randomized within a participant in the same order across participants)

Navon Hierarchical Figure Letter Pairs

Morphologically Similar	Morphologically Dissimilar
FE	ON
JU	LC
VW	KM
MN	ET
AH	XS
NM	AJ
BP	EO
IT	RN
TI	HZ
UJ	NR
EF	OE
LE	ZH
OC	NO
XK	MK
WV	HX
HA	CL
CO	TE
KX	SX
PB	XH
EL	JA

Navon Practice Condition. All participants completed a *Navon practice* condition consisting of 10 trials prior to the test condition. Modeling Koldewyn and colleagues' (2013) work, all images included objects or pictures. Importantly, while Koldewyn's practice trials involved training their participants' to match categories with a clear correct versus incorrect match (e.g., dog sample, different dog target and flower distractor), the images presented during this practice condition involved unique images within the *same* category with a more ambiguous match (e.g., lion sample, lioness target and dog distractor). Given that neither of the two options are identical, participants are able to use whatever clues they would like to make their selection (global shapes, colors, detail differences), but the global category (i.e., animals) is not relevant. This ensured that the practice trial did not facilitate in training categorization of the global percept, but ensured mastery of the concept of a match-to-sample paradigm instead.

Navon Test Condition. One test condition of 40 trials was administered, which included hierarchical Navon letters as described above. Participants were required to select one of two Navon hierarchical figures that matched the previously presented non-Navon letter (i.e., a real letter)—one Navon figure was the "global match" (i.e., the large letter matched the sample real letter, and was comprised of smaller incongruent letters), and the other was the "local match" (i.e., the small letters matched the sample real letter, which were aligned to form an incongruent non-match larger letter). The Navon hierarchical figures always appeared on each side of the midline. The position of the Navon figures did not change across trials. Morphologically *similar* and *dissimilar* letter pairs were pseudo-randomized such that letter pairs were randomly presented in the same order for each participant. Letter pairs repeated only once across the 40 trails, with the target letter switching to represent the letter not previously presented (e.g., K for

KM, and then M for KM letter pair). Category of letter pairs (i.e., morphologically *similar* or *dissimilar*) appeared no more than three consecutive trials. Smiley face reinforcement and verbal encouragement was administered similarly to the KIC test conditions.

Eye-tracking Procedures.

Areas of Interest (AOI)

KIC Paradigm. Based on prior work (Guttman & Kellman, 2004; Nayar et al., 2017; Ringach & Shapley, 1996), attention allocated to the individual pacman elements comprising the KIC figure implicated local perceptual processes, while attention to the centers of the KIC forms indicated global perceptual processes. As such, there were two primary operationally defined AOIs (*Fig. 3.2*): the centers of the illusory contours and their pacman elements. Pacman AOI was defined consistent with our prior work (Nayar et al., 2017), such that attention allocated to the physical pacman element plus the empty pie was considered local processing. KIC center AOI was defined as the space induced by the pacman elements within the illusory boundaries and not including the empty pie. For the *KIC noise* test condition only, any attention to the background pacman elements was additionally considered to be local processing. Although the *KIC noise* test condition includes an aspect of search demand, it is not a classic visual search paradigm as it requires the integration of local pacman elements to create the global illusory form, which is embedded within an array of jittered pacman elements. As such, the background pacman elements offer a local interference effect. Finally, the target (match) and non-target (non-match) KIC forms were additionally defined.

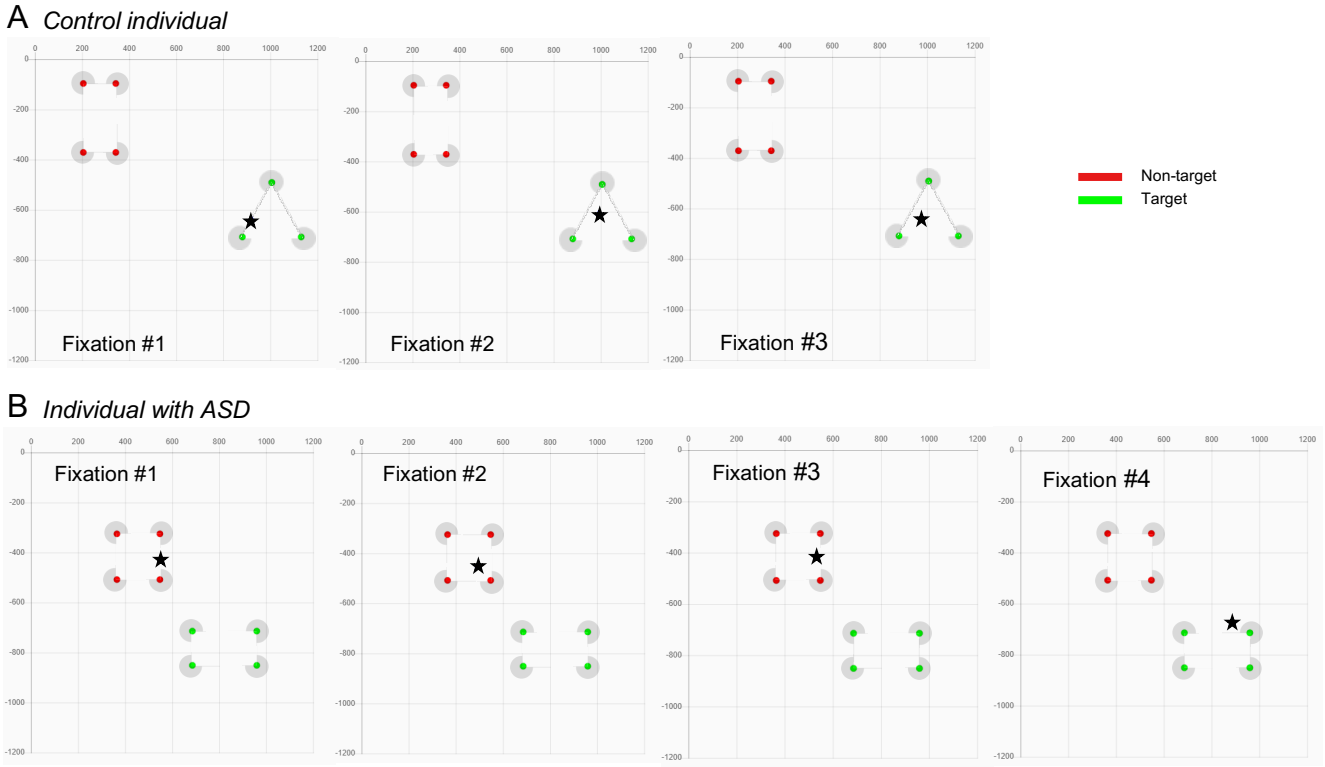

Figure 3.2. *A series of images depicting eye tracking trajectories during the KIC Paradigm between an individual with ASD compared to a control individual. Red KIC is the non-target image and the green KIC is the target match. Star depicts location of fixation. A) A panel depicting a control individual making 3 consecutive fixations to the target before selecting the match. B) panel depicting an individual with ASD making 3 consecutive fixations to the non-target before fixating on the target.*

Navon Paradigm. AOIs defined in the *Navon test* condition were relatively straightforward and only included 2 AOIs: the "global" match and the "local" match. A rectangular figure within the bounds of the stimulus surrounded the Navon figure and defined the global or local match AOIs.

Quality control procedures

Fixations were defined in a manner consistent with prior work (Wass et al., 2013) to account for potential data loss, and accordingly adjusted to account for the short durations associated with each trial of the match-to-sample paradigms. Pre-defined settings in Tobii Studio were customized to reduce the impact of technological error or intra-individual variability (such as the tendency for the eyes to move towards the edge of the screen, flicker and inconsistent gaze data, or head movement). As such, fixations were defined based on the I-VT fixation filter available in Tobii Studio, which included the following fixation settings: 1) minimum fixation duration of 100ms; 2) fixation data were averaged across both eyes, 3) velocity threshold of 20°/s, 4) maximum duration and angle between each new fixation were set at 100 ms and 0.5°, respectively, 5) moving average window of 3 samples was included to reduce noise, and 6) missing data with gaps of maximum 150 ms were linearly interpolated. Additionally, a valid trial was defined as having a minimum of 1 fixation count and a valid participant was defined as having a minimum of 50% valid trials of total trials (i.e., a minimum of 20 valid trials). In order to maximize sample size to examine group differences, a participant was included in final analyses if they presented with at least one valid *KIC basic* and/or *KIC noise* trial for the *KIC paradigm*.

No significant group differences emerged between groups in the average number of valid trials across conditions (*KIC Paradigm across test conditions*: ASD group—M (SD) = 36.6 (4.9), control group—M (SD) = 36.9 (4.3), t (108) = .32, p = .75; ASD parent group—M (SD) = 38.7 (2.7), Parent control group—M (SD) = 39.0 (2.0), t (193) = 1.15, p = .25. *Navon Paradigm*: ASD group—M (SD) = 35.1 (5.8), control group—M (SD) = 37.7 (3.5), t (35.30) = 1.78, p = .08; ASD parent group—M (SD) = 36.4 (5.4); Parent control group—M (SD) = 36.4 (4.5), t (84) = -.02, p = .99). As such, N trials was not included as a covariate in statistical analyses (see below).

In addition to the above quality control settings, consistent with prior work (e.g., Anderson et al., 2006), each AOI had a "buffer" area based on proportionally expanding the AOI's original size by 20%. For the *KIC basic* and *KIC noise* conditions, pacman elements were expanded by increasing the radius by 20% while maintaining the original (x, y) coordinates. For the area defined by the KIC center, a dilation ratio of 1.2 (i.e., 20%) was utilized to expand this area by 20% around the center's (x, y) coordinates. For the *Navon test* condition, each rectangular AOI encompassing the Navon figure was expanded by a dilation ratio of 1.2 based on its center (x, y) coordinates.

Variables of Interest

Refer to Table 3.3 for condensed descriptions and overview of variables included in analyses across tasks.

Table 3.3: Definitions of KIC and Navon performance and gaze variables and composites

	Variable Definition (KIC)	Variable Definition Navon
Performance-based variables		
Accuracy	Percent correct based on target click	Percent correct based on target (i.e., global) click (only present for overall Navon analyses)
Reaction Time	Average reaction time in second per trial	Average reaction time in second per trial
Strategy-based gaze variables		
Exploration	Average number of fixations per second per trial	Average number of fixations per second per trial
Vacillations	Average percent of transition fixations between target versus non-target stimuli	Average percent of transition fixations between target versus non-target stimuli
Center-Pacman Difference (i.e., Diff) Composite	Average percent difference between center and pacman looks (higher value indicates a greater percentage of center looks)	-
Center-Pacman Diff First Fixation	Average percent difference of first fixations made towards KIC centers versus pacman first fixations (higher value indicates a greater percentage of center first fixations)	-
Center-Pacman Diff Fixation	Average percent difference of fixations made towards KIC centers versus pacman fixations (higher value indicates a greater percentage of center fixations)	-
Center-Pacman Diff Fixation Duration	Average percent difference of fixation duration spent attending towards KIC centers versus pacman elements (higher value indicates a greater percentage of time allocated towards KIC centers)	-
Target-Non-Target Diff Composite	Average percent difference between target and non-target looks (higher value indicates a greater percentage of target looks)	Average percent difference between target and non-target looks (higher value indicates a greater percentage of target looks)

Target-Non-Target Diff First Fixation	Average percent difference of first fixations made towards the target KIC versus the non-target KIC (higher value indicates a greater percentage of target first fixations)	Average percent difference of first fixations made towards the target/global Navon versus the non-target/local Navon (higher value indicates a greater percentage of target first fixations)
Target-Non-Target Diff Fixation	Average percent difference of fixations made towards the target KIC versus the non-target KIC (higher value indicates a greater percentage of target match fixations)	Average percent difference of fixations made towards the target/global Navon versus the non-target/local Navon (higher value indicates a greater percentage of target fixations)
Target-Non-Target Diff Fixation Duration	Average percent difference of fixation duration spent attending towards the target KIC versus the non-target KIC (higher value indicates a greater percentage of time allocated toward the target match).	Average percent difference of fixation duration spent attending towards the target/global Navon versus the non-target/local Navon (higher value indicates a greater percentage of time allocated toward the targe Navon stimulus)
Composite score		
Global-Local Diff Composite	Average z-scored sum of accuracy, reaction time, target and center percent first fixations, fixations, and duration minus the z-scored sum of the non-target and pacman element first fixations, fixations, and duration as well as percent vacillations and exploration (higher value indicates greater "global" than "local" processing)	Average z-scored sum of accuracy, reaction time, target percent first fixations, fixations, and duration minus the z-scored sum of the non-target first fixations, fixations, and duration as well as percent vacillations and exploration (higher value indicates greater "global" than "local" processing)

Performance-based variables

1. Percent Accuracy or Global Match. For the KIC paradigm, accuracy was defined as the total number of correct responses (i.e., selecting the target KIC that matched the non-illusory sample shape), divided by the total number of trials included in the condition multiplied by 100. For the Navon paradigm, the percentage of trials in which the participant selected the "global match" was explored. Due to online data collection methods, accuracy was only determined for the entire Navon task (and not by Navon stimulus type).

2. Reaction Time. While not as accurate as utilizing a touch screen (Nayar et al., 2015; Nayar et al., 2017), reaction time (in sec) was determined based on the time between the presentation of the two KIC target/non-target options or the two Navon figures and the instant the participant clicked the computer mouse to make their selection.

Strategy-based gaze variables

1. Exploration. The total number of fixations that occurred throughout the duration of the trial, divided by the total track time (in seconds).

2. Percent Vacillation. The total number of vacillations that occurred between the target/non-target KIC or the two Navon options was summed for each individual trial, divided by the total number of trials included for that condition, and multiplied by 100.

Center-Pacman Difference Scores - for *KIC Test Conditions only*.

For the following variables, pacman elements for the *KIC basic* test condition included the pacman inducers to the KIC only, while for the *KIC noise* test condition, pacman elements

also included the background individual pacman elements. The below were computed for each test condition separately. Additionally, higher values indicate greater center gaze allocation.

1. First Fixation. The average difference between the percentage of first fixations for each trial that was towards the KIC center minus pacman element (higher value indicates a greater percentage of center first fixations).

2. Fixation. The average difference between the percentage of fixations for each trial made towards the KIC centers minus the percentage of fixations made towards the pacman elements (higher value indicates a greater percentage of center fixations).

3. Duration. The average difference between the percentage of time spent for each trial looking towards the KIC centers minus the percentage of time spent looking at the pacman elements (higher value indicates a greater percentage of time spent looking at the center).

Target-NonTarget Difference Scores.

Higher values in the below variables reflect greater target gaze.

1. First Fixation. The average difference between the percentage of first fixations for each trial that was towards the target match minus the non-target option (higher value indicates a greater percentage of target first fixations).

2. Fixation. The average difference between the percentage of fixations for each trial made towards the target match minus the percentage of fixations made towards the non-target option (higher value indicates a greater percentage of target fixations).

3. Duration. The average difference between the percentage of time spent for each trial looking towards the target minus the percentage of time spent looking at the non-target stimulus (higher value indicates a greater percentage of time spent looking at the target).

Composite Gaze Variables.

Higher values in the below variables indicate greater center or target gaze (i.e., greater propensity for global processing).

1. Center-Pacman Difference Score: For the KIC paradigm only, the center-pacman difference composite score is the average of the sum of center percent first fixations, fixations, and duration minus the sum of the pacman first fixations, fixations, and duration.

2. Target-NonTarget Difference Score: The average of the sum of target percent first fixations, fixations, and duration minus the sum of the non-target first fixations, fixations, and duration.

Overall Composite Global-Local Difference Score

Overall Global-Local Difference Score (z-score difference): For both paradigms, this composite score was generated to reflect an overall difference between global and local processing styles. The score included all variables outlined above as follows. All variables were first converted to z-scores to ensure that all variables were of comparable scale. For the *KIC Paradigm*, this composite variable is the average sum of the z-scored accuracy, reaction time (reverse coded to ensure comparable theoretical directionality of z-scores across variables), target and center percent first fixations, fixations, and duration minus the sum of the z-scored

non-target and pacman element first fixations, fixations, and duration as well as percent vacillations and exploration. For the *Navon Paradigm*, this composite variable is the average sum of the z-scored accuracy, reaction time (reverse coded), target percent first fixations, fixations, and duration minus the sum of the z-scored non-target first fixations, fixations, and duration as well as percent vacillations and exploration.

Statistical Analysis

Quality Control Procedures

Assumptions testing. Data were examined to assess model assumptions. Outlier examination revealed that one ASD parent (father) was identified as a relatively consistent extreme outlier across most KIC variables and was therefore removed from subsequent analyses. There were no consistent extreme outliers in the Navon task. Assumptions for linear mixed effect models (see below) were appropriately met across most variables as follows: 1) residual errors were all normally distributed following Q-Q plot examination, 2) most variables' variances were homogeneous based on Levene's tests, with the exception of most performance variables across tasks and parent/proband groups, 3) all residuals were linear, and 4) variables were co-linear for tasks within conditions (i.e., *KIC basic* and *KIC noise* for the KIC task, and *similar* versus *dissimilar* letters for the Navon task). Given failed homogeneity of variance on accuracy and reaction time measures overall, performance variables were re-analyzed using non-parametric tests (Mann-Whitney U).

Covariates. Covariates were examined using theoretical and data-driven approaches.

For probands, given that IQ was significantly different between diagnostic groups (see *Table 3.1*), and known relationships between cognitive abilities and performance across neuropsychological tasks in ASD (Rommelse et al., 2015), IQ was added as a covariate for accuracy and reaction time analyses across tasks. Although IQ correlated with *eye-tracking* variables in proband groups, final models did not include IQ as a covariate for gaze indices, as 1) results did not differ when analyses were conducted with or without controlling IQ, and 2) given that differences in IQ is associated with the inherent heterogeneity in ASD, it is important to allow for variability within the group when assessing discriminability of potential diagnostic classifiers (Dennis et al., 2009). Age was not included as a covariate for proband analyses given no significant differences between groups or associations with outcome variables.

For parents only, age significantly correlated with outcome variables across both KIC and Navon paradigms. As such, analyses were conducted with and without age included as a covariate in all parent analyses. Significance did not differ between models (results not shown), and as such, all reported parent analyses include models *without* age as a control variable. Although IQ was significantly different between parent groups, it did not correlate with outcome variables and was therefore not controlled for in parent analyses.

1. Assessment of Group Differences in Local/Global Perception Tasks

For both paradigms, parent groups and proband groups were analyzed separately. Group differences in performance and gaze variables were assessed using a series of mixed effects linear regression models using the lmer package (Bates, Mächler, Bolker, & Walker, 2014) *R Studio* (Team, 2019) to assess the effect of condition, group, and the interaction. Models for the KIC paradigm included diagnostic group (control group as the reference group) and condition

(*Basic KIC* and *KIC Noise,* with the *Basic KIC* condition as the reference group) as fixed effects, as well as their interaction term. For Navon, primary analyses included examining group differences only across all trials using ANCOVA or ANOVA, with the above-mentioned covariates. Secondary more exploratory analyses further examined effects of morphologically *similar* or *dissimilar* letters as follows: A series of linear mixed effect models with diagnostic group (control as the reference group) and letter similarity (*dissimilar* and *similar*, with dissimilar as the reference group) were included as the fixed effects, as well as their interaction. Across all models, the individual participant was included as the random effect. Interaction terms were only interpreted if there was a significant improvement in model fit, with the models being run with and without the interaction term. If there was no improvement in model fit with the addition of the interaction term, only main effects were interpreted. Finally, if the interaction term was significant, only this 2-way interaction finding was reported and interpreted, without main effects of group or condition separately.

To explore cross-task differences, for each participant, overlapping variables were averaged first between the KIC conditions (*KIC basic* and *KIC noise* conditions) and then between paradigms (KIC and Navon), to generate an average value for composite gaze and overall composite variables only (i.e., *Target-NonTarget Difference Composite score* and *Global-Local Difference Composite* z-score). A series of ANOVAs were examined to explore group differences in local or global processing across tasks.

Group differences including performance (i.e., accuracy and reaction time) and gaze composite variables (5 variables total for the KIC paradigm, and 4 for the Navon paradigm) were examined as a first level of analyses, followed by more exploratory analyses involving individual

gaze variables comprising composite variables (i.e., exploration, vacillation, and difference scores) in order to examine more comprehensively the nature of differences potentially found in composite scores. Group differences were adjusted using the Benjamini-Hochberg method (Benjamini & Hochberg, 1995) using a FDR of .10 to reduce false negatives and thereby potentially missing important effects (APA, 1994b). Benjamini-Hochberg adjusted *p* values are reported in Tables 3.4 – 3.9; all other *p* values meeting an alpha criterion of < .05 are reported below.

Finally, in order to examine how performance and gaze variables related to each other, within-task associations for KIC and Navon Paradigms between gaze composite variables (i.e., *Vacillation*, *Exploration*, and composite *Center-Pacman Difference* and *Target-NonTarget Difference scores*) and performance variables (accuracy and reaction time) were examined across groups separately for parents and probands. *The Overall Global-Local Difference Score* was not included in association models given that it is comprised of all gaze and performance variables. For probands, to remain consistent with overall group models, IQ was included as a covariate, and a series of partial Pearson correlations were conducted. For the KIC paradigm, both conditions were averaged for the purpose of being parsimonious. Finally, accuracy and reaction time associations were explored to assess whether speed of response, impacted accuracy (particularly given that global processing is rapid). Due to most performance variables failing Levene's test of homogeneity of variance, Pearson correlations were followed-up with bivariate Spearman's rank-order partial correlations.

2. Analyses of Parent-child Associations in Local/Global Perception Tasks

To explore whether profiles of local and global processing may show a pattern of familiality, linear regression models were employed separately for each family diagnosis on composite variables across tasks only (i.e., using the across-task averaged composite variable—*Overall Global-Local Difference Score*) between parent and child pairs. All models included within-family relation nested within the model as a random effect to control for spousal relationships with the same child. These analyses were exploratory given small sample sizes (ASD dyads n = 11; Control dyads n = 20). Additionally, in order to examine whether local/global processing may confer familiality or simply reflect ASD-risk more broadly, parent-child associations were re-run with unrelated, mismatched parent-child dyads. A randomization/Permutation (Katz, Lautenschlager, Blackburn, & Harris, 1990) test using a series of *Pearson*'s correlations between unrelated mother-child dyads was applied to evaluate the specificity of familial relationships. Each parent value was randomly paired with a child's value for all possible permutations within each diagnostic group, which resulted in a sampling distribution of the correlation coefficients. Based on this test, the expected correlation coefficient is zero. The permutations test resulted in a distribution of all possible permutations of unrelated pairs within diagnostic groups. Subsequently, the strength of the true parent-child dyad correlation coefficient was compared against the distribution for the unrelated pairs (i.e., true ASD parent-child dyads versus all unrelated ASD pairings, and true control parent-child dyads versus all unrelated control pairings). Final metrics included a probability statistic that indicated the likelihood of any random pairing producing a stronger correlation coefficient relative to the true parent-child dyad correlation coefficient.

3. Relationships with Clinical-Behavioral Correlates in Local/Global Perception Tasks

Using the across-task averaged variables, Pearson correlations were examined between performance, gaze, and composite variables and clinical-behavioral and cognitive correlates. For probands, partial Pearson correlations were conducted with IQ added as a covariate for correlations between performance and clinical-behavioral characteristics. Associations with clinical-behavioral traits involving ASD or BAP measures were only examined in clinical groups (i.e., ASD and ASD parent groups).

Clinical-Behavioral Correlates

For individuals with ASD, the ADOS total and subscale (social affect and restricted and repetitive behaviors) calibrated severity scores, ADI current domain and total scores, SRS total T-score, and RBS-R Overall Sum were all utilized in correlations with cross-task variables. Rates of pragmatic language violations (PRS-SA Total and domain scores—e.g., *theory of mind domain*, which includes items that tap theory of mind skills during conversation such as being unable to clarify, failing to provide background, being redundant, being detail oriented) were examined in both ASD and control groups separately.

For parents of individuals with ASD, BAPQ total and sub-scores (i.e., pragmatic, aloof, and rigid) were examined in relation to local and global processing. Similar to individuals with ASD, the PRS total and factor scores (i.e., *dominating conversation* factor score—which is a sum of items including being overly detailed, being tangential, being frank, exhibiting odd humor, and demonstrating optic preoccupation—and *socially withdrawn* factor score, which includes

items such as being vague, being unable to clarify responses, failing to reciprocate, and failing to elaborate on their responses) were examined for both the ASD parent and parent control groups.

Cognitive Correlates

Social cognition (as measured by The Reading the Mind in the Eyes Test percent correct) and measures of executive functioning (Flanker age-corrected Standard Score and BRIEF GEC T-score) were also examined in both ASD and control families separately.

Results

The results section is organized to include findings in 1) The overall composite gaze score (i.e., the *Overall Global-Local Composite Score)*, 2) performance-based variables (accuracy and reaction time), and 3) strategy-based gaze variables. Within the strategy-based gaze variables results section, findings from individual gaze variables (i.e., center-pacman first fixation, fixation, and fixation duration difference scores and/or target-nontarget first fixation, fixation, and fixation duration difference scores) are described. All statistics are reported in relevant tables. Finally, given known differences between KIC test conditions (basic versus noise) (Nayar et al., 2017) and not central to primary aims of the study, condition effects are reported in Tables 3.4 and 3.5 only, and not in the text below. Additionally, although condition and group X condition effects during the Navon paradigm were exploratory in nature, results from condition effects are also only reported in Tables 3.8 and 3.9.

1. Group Differences

KIC Paradigm (Tables 3.4 - 3.5; Fig. 3.3)

Overall Composite Global-Local Difference Score

ASD vs. Controls: A main effect of group emerged, showing that the ASD group demonstrated reduced global perception overall across conditions than did the control group.

ASD parent vs. parent controls: No main effect of group was found between parent groups.

Performance-based variables

Accuracy.

ASD vs. Controls: There were no main effects of group or a group X condition interaction. Non-parametric analyses demonstrated significant group differences in the *KIC basic* condition, showing lower means in the ASD (M_{rank} = 21.25) versus control (M_{rank} = 31) group (U = 210, $p < .05$). Similar trends were observed in the *KIC noise* condition showing relatively lower means among individuals with ASD (M_{rank} = 25.38) compared to the control group (M_{rank} = 33.35) (U = 304.5, p = .05).

ASD parent vs. parent controls: Likewise, no group or interaction effects emerged for accuracy in parents. Non-parametric results revealed lower means in the ASD parent group (M_{rank} = 43.72) compared to the parent control group (M_{rank} = 54.40) (U = 886, $p < .05$). In contrast, no group differences emerged in the *KIC noise* condition (parent control group M_{rank} = 51.31, ASD parent group M_{rank} = 43.72, U = 1058, p = .43).

Reaction Time.

ASD vs. Controls: No group main effect or group X condition interaction effect emerged for reaction time in proband groups. Non-parametric Mann-Whitney U tests revealed significant group differences across both conditions, showing slower means in the ASD (*KIC basic* M_{rank} = 22.11; *KIC noise* M_{rank} = 22.47) compared to the control (*KIC basic* M_{rank} = 31.63; *KIC noise* M_{rank} = 37.04) group (*KIC basic* $U = 213$, $p < .05$; *KIC noise* $U = 209$, $p = .001$).

ASD parent vs. parent controls: A main effect of group showed that the ASD parent group were slower to respond than the control parent group. There was no group X condition interaction. Non-parametric test similarly revealed significant group differences in mean ranks between groups, particularly during the *KIC basic* condition (parent control group M_{rank} = 38.40, ASD parent group M_{rank} = 56.70, $U = 1651$, $p = .001$). Similar trends were observed in the *KIC noise* condition showing that the ASD parent group (M_{rank} = 53.56) responded relatively slower than the parent control group (M_{rank} = 43.02) ($U = 904$, $p = .07$).

Strategy-based gaze variables

Exploration.

ASD vs. Controls: There was a main effect of group, showing that the ASD group had elevated exploration rates (i.e., made a significantly greater number of fixations per second) than the control group.

ASD parent vs. parent controls: No main effects of group or group X condition interaction emerged for parents.

Percent Vacillation.

ASD vs. Controls: There was a main effect of group and group X condition interaction, showing that the ASD group vacillated more than the control group, particularly during the KIC basic condition.

ASD parent vs. parent controls: No group or interaction effects emerged between parent groups.

Center-Pacman Difference Score.

ASD vs. Controls: While no overall main effects of group or interaction emerged for the overall composite score, a group X condition effect was found for the percentage of *fixation* and *fixation duration* center-pacman difference variables—both gaze variables showed a greater percentage of fixations and time spent on KIC centers versus pacman elements during the KIC basic versus KIC noise condition across groups, which was attenuated for the ASD group compared to the control group, and with more pronounced group differences emerging in the KIC noise condition.

ASD parent vs. parent controls: A group X condition effect emerged for parents, showing a higher percentage of KIC center versus pacman perception during the KIC basic versus KIC noise condition across groups. Importantly, between-group patterns differed based on condition showing that the ASD parent group attended more towards the center versus pacman during the KIC basic condition compared to controls, which was flipped for the KIC noise condition (where both groups attended more towards pacman elements, with the ASD parent group showing even greater pacman versus center attention than the parent control group). This group X condition interaction was driven by the percentage of *fixation* and *fixation duration* variables.

Target-NonTarget Difference Score.

ASD vs. Controls: Across conditions, the ASD group attended less towards the target versus the non-target KIC compared to the control group, a pattern that was evident across all variables comprising this composite variable. Additionally, a group X condition interaction revealed a greater percentage of target fixations and increased time spent looking at the target versus the non-target KIC during the KIC basic versus the KIC noise condition across groups, and that the ASD group overall demonstrated reduced target versus non-target fixations and fixation duration compared to the control group.

ASD parent vs. parent controls: Parent findings were similar to those in probands, showing a main effect of group, such that the ASD parent group showed less attention towards target versus non-target KICs (particularly showing reduced *percent* fixation and *percent fixation duration)* compared to the parent control group across conditions.

Table 3.4: *Summary of KIC Results- ASD versus Control groups*

	Control Group		**ASD Group**	
	KIC Basic M (SE)	**KIC Noise** M (SE)	**KIC Basic** M (SE)	**KIC Noise** M (SE)
Performance-based variables				
Accuracy^	97.80 (0.89)	97.30 (0.86)	96.00 (0.96)	96.00 (0.91)
Reaction Time^ (s)	.84 (0.08)	1.24 (0.08)	1.06 (0.09)	1.63 (0.08)
Strategy-based gaze variables				
Exploration	3.38 (0.10)	3.63 (0.10)	3.61 (0.10)	4.00 (0.11)
Vacillations	20.12 (1.41)	14.29 (0.89)	25.91 (2.13)	15.05 (0.60)
Center-Pacman Diff Composite	13.73 (4.85)	-27.38 (3.6)	8.27 (3.91)	-44.72 (3.97)
Center-Pacman Diff First Fixation	19.14 (4.44)	-22.58 (3.31)	15.98 (4.27)	-39.84 (3.78)
Center-Pacman Diff Fixation	23.81 (4.79)	-13.16 (3.69)	18.85 (4.88)	-33.35 (4.68)
Center-Pacman Diff Fixation Duration	9.02 (4.33)	-49.29 (4.45)	-0.7 (3.05)	-61.31 (3.31)
Target-Non-Target Diff Composite	50.25 (2.76)	41.41 (2.14)	34.83 (2.51)	28.29 (2.30)
Target-Non-Target Diff First Fixation	49.68 (2.36)	42.42 (2.07)	36.73 (2.59)	30.59 (2.25)
Target-Non-Target Diff Fixation	63.14 (2.51)	56.57 (1.99)	47.79 (3.05)	40.33 (2.70)
Target-Non-Target Diff Fixation Duration	37.92 (4.02)	25.24 (2.90)	19.97 (2.54)	13.94 (2.62)
Composite z-score				
Global-Local Diff Composite	0.98 (0.16)	0.05 (0.15)	-0.02 (0.20)	-1.02 (0.18)

ASD versus control groups	*Est.*	β	*SE*	*df*	*t*	*p*	*padj*
			Main Effect of Group				
Performance-based variables							
Accuracy^	-1.82	-0.19	1.39	82.14	-1.32	0.192	0.250
Reaction Time^ (s)	0.22	0.19	0.13	76.63	1.73	0.088	0.132
Strategy-based gaze variables							
Exploration	0.34	0.29	0.15	80.67	2.25	**0.027**	**0.048**
Vacillations	5.64	0.35	1.90	103.81	2.96	**0.004**	**0.008**
Center-Pacman Diff Composite	-5.32	-0.08	5.88	95.31	-0.91	0.368	0.463
Center-Pacman Diff First Fixation	-9.31	-0.13	5.66	97.72	-1.64	0.104	0.144
Center-Pacman Diff Fixation	-2.93	-0.05	5.64	96.27	-0.52	0.604	0.693
Center-Pacman Diff Fixation Duration	-5.25	-0.08	6.37	91.06	-0.82	0.412	0.503
Target-Non-Target Diff Composite	-14.28	-0.48	3.45	88.76	-4.14	**0.000**	**0.000**
Target-Non-Target Diff First Fixation	-17.00	-0.46	4.47	95.89	-3.80	**0.000**	**0.001**
Target-Non-Target Diff Fixation	-11.60	-0.42	3.27	89.17	-3.54	**0.001**	**0.002**
Target-Non-Target Diff Fixation Duration	-14.44	-0.46	3.57	85.25	-4.04	**0.000**	**0.001**
Composite z-score							
Global-Local Diff Composite	-0.99	-0.43	0.24	86.24	-4.07	**0.000**	**0.000**
			Main Effect of Condition				
Performance-based variables							
Accuracy^	-0.51	-0.05	0.80	46.33	-0.64	0.526	0.622
Reaction Time^ (s)	0.41	0.46	0.07	44.53	6.13	**0.000**	**0.000**
Strategy-based gaze variables							
Exploration	0.28	0.24	0.08	45.57	3.44	**0.001**	**0.003**
Vacillations	-5.92	-0.36	1.59	49.99	-3.72	**0.001**	**0.002**
Center-Pacman Diff Composite	-41.09	-0.64	4.05	49.80	-10.16	**0.000**	**0.000**
Center-Pacman Diff First Fixation	-58.60	-0.80	4.16	47.06	-14.07	**0.000**	**0.000**

Center-Pacman Diff Fixation	-41.49	-0.64	3.95	49.97	-10.50	**0.000**	**0.000**
Center-Pacman Diff Fixation Duration	-36.96	-0.56	4.04	49.13	-9.15	**0.000**	**0.000**
Target-Non-Target Diff Composite	-8.77	-0.29	2.11	48.08	-4.16	**0.000**	**0.001**
Target-Non-Target Diff First Fixation	-12.64	-0.34	3.14	48.76	-4.03	**0.000**	**0.001**
Target-Non-Target Diff Fixation	-6.96	-0.25	2.02	48.17	-3.45	**0.001**	**0.003**
Target-Non-Target Diff Fixation Duration	-6.74	-0.21	2.01	48.58	-3.35	**0.002**	**0.004**
Composite z-score							
Global-Local Diff Composite	-0.93	-0.41	0.14	48.40	-6.61	**0.000**	**0.000**
	Group X Condition Interaction						
Performance-based variables							
Accuracy^	0.56	0.05	1.20	49.84	0.47	0.643	0.697
Reaction Time^ (s)	0.17	0.09	0.10	47.53	1.67	0.101	0.144
Strategy-based gaze variables							
Exploration	0.03	0.02	0.12	48.06	0.23	0.818	0.818
Vacillations	-5.03	-0.27	2.34	54.66	-2.15	**0.036**	0.061
Center-Pacman Diff Composite	-11.86	-0.16	6.02	53.60	-1.97	0.054	0.085
Center-Pacman Diff First Fixation	-3.07	-0.04	6.18	51.18	-0.50	0.622	0.693
Center-Pacman Diff Fixation	-14.25	-0.19	5.88	53.87	-2.43	**0.019**	**0.037**
Center-Pacman Diff Fixation Duration	-14.58	-0.19	6.04	52.51	-2.42	**0.019**	**0.037**
Target-Non-Target Diff Composite	1.15	0.03	3.16	51.25	0.36	0.717	0.736
Target-Non-Target Diff First Fixation	5.71	0.14	2.19	56.40	-1.49	0.141	0.190
Target-Non-Target Diff Fixation	-0.20	-0.01	1.61	53.46	-2.12	**0.038**	0.062
Target-Non-Target Diff Fixation Duration	-1.84	-0.05	1.46	53.66	-2.28	**0.026**	**0.048**
Composite z-score							
Global-Local Diff Composite	-0.08	-0.03	0.21	51.30	-0.39	0.699	0.736

Bold $p < .05$; padj reflects the Benjamini-Hochberg correction at a false discovery rate of .10; ^IQ added as a covariate

Table 3.5: *Summary of KIC Results - ASD parent versus parent control groups*

	Parent Control Group		**ASD Parent Group**	
	KIC Basic M (SE)	**KIC Noise** M (SE)	**KIC Basic** M (SE)	**KIC Noise** M (SE)
Performance-based variables				
Accuracy	99.00 (0.3)	99.00 (0.23)	98.32 (0.32)	98.38 (0.32)
Reaction Time	0.83 (0.03)	1.35 (0.05)	0.96 (0.02)	1.55 (0.07)
Strategy-based gaze variables				
Exploration	3.43 (0.07)	3.73 (0.07)	3.50 (0.07)	3.75 (0.06)
Vacillations	24.74 (1.40)	14.85 (0.47)	22.37 (1.44)	16.11 (0.48)
Center-Pacman Diff Composite	6.66 (2.68)	-40.5 (2.39)	9.58 (2.42)	-44.82 (2.01)
Center-Pacman Diff First Fixation	12.69 (2.85)	-33.02 (2.45)	15.14 (2.58)	-37.94 (2.12)
Center-Pacman Diff Fixation	17.35 (3.10)	-24.43 (2.74)	20.29 (2.87)	-29.48 (2.42)
Center-Pacman Diff Fixation Duration	-2.07 (2.52)	-67.47 (2.49)	-1.23 (2.43)	-70.99 (2.12)
Target-Non-Target Diff Composite	39.3 (1.97)	32.37 (1.01)	34.38 (1.63)	29.23 (1.10)
Target-Non-Target Diff First Fixation	40.98 (1.94)	35.36 (1.14)	36.22 (1.53)	32.2 (1.18)
Target-Non-Target Diff Fixation	56.74 (1.86)	48.45 (1.23)	50.66 (1.77)	44.45 (1.39)
Target-Non-Target Diff Fixation Duration	20.18 (2.61)	13.31 (1.42)	16.25 (2.17)	11.03 (1.40)
Composite z-score				
Global-Local Diff Composite	0.60 (0.14)	-0.32 (0.09)	0.42 (0.11)	-0.64 (0.10)

Bold $p < .05$; padj reflects the Benjamini-Hochberg correction at a false discovery rate of .10

ASD parent versus parent control groups	*Est.*	β	*SE*	*df*	*t*	*p*	*padj*
			Main Effect of Group				
Performance-based variables							
Accuracy	-0.72	-0.17	0.43	171.03	-1.65	0.101	0.187
Reaction Time (s)	0.17	0.19	0.08	121.51	2.25	**0.027**	**0.065**
Strategy-based gaze variables							
Exploration	0.09	0.09	0.09	131.70	0.92	0.361	0.522
Vacillations	-2.37	-0.14	1.52	188.99	-1.56	0.121	0.215
Center-Pacman Diff Composite	2.79	0.05	3.36	154.75	0.83	0.408	0.548
Center-Pacman Diff First Fixation	0.97	0.01	3.40	174.64	0.29	0.775	0.817
Center-Pacman Diff Fixation	2.12	0.03	3.55	147.30	0.60	0.551	0.632
Center-Pacman Diff Fixation Duration	2.59	0.04	3.95	146.37	0.66	0.513	0.606
Target-Non-Target Diff Composite	-5.06	-0.23	2.09	157.10	-2.42	**0.017**	**0.047**
Target-Non-Target Diff First Fixation	-3.82	-0.14	2.78	172.00	-1.38	0.171	0.290
Target-Non-Target Diff Fixation	-4.99	-0.24	2.09	159.64	-2.39	**0.018**	**0.047**
Target-Non-Target Diff Fixation Duration	-6.46	-0.27	2.28	148.01	-2.83	**0.005**	**0.017**
Composite z-score							
Global-Local Diff Composite	-0.20	-0.11	0.16	152.51	-1.24	0.216	0.352
			Main Effect of Condition				
Performance-based variables							
Accuracy	0.01	0.00	0.38	92.53	0.02	0.983	0.983
Reaction Time (s)	0.52	0.60	0.05	78.12	10.78	**0.000**	**0.000**
Strategy-based gaze variables							
Exploration	0.29	0.30	0.06	92.95	5.01	**0.000**	**0.000**
Vacillations	-9.89	-0.59	1.60	96.06	-6.18	**0.000**	**0.000**
Center-Pacman Diff Composite	-46.86	-0.77	2.56	94.04	-18.33	**0.000**	**0.000**
Center-Pacman Diff First Fixation	-65.19	-0.86	3.02	93.48	-21.58	**0.000**	**0.000**

Center-Pacman Diff Fixation	-45.51	-0.75	2.53	93.87	-18.00	**0.000**	**0.000**
Center-Pacman Diff Fixation Duration	-41.53	-0.69	2.79	93.92	-14.88	**0.000**	**0.000**
Target-Non-Target Diff Composite	-6.64	-0.31	1.64	92.06	-4.05	**0.000**	**0.000**
Target-Non-Target Diff First Fixation	-6.59	-0.24	2.43	91.60	-2.71	**0.008**	**0.024**
Target-Non-Target Diff Fixation	-5.43	-0.26	1.67	92.27	-3.26	**0.002**	**0.005**
Target-Non-Target Diff Fixation Duration	-8.00	-0.34	1.67	91.06	-4.80	**0.000**	**0.000**
Composite z-score							
Global-Local Diff Composite	-0.89	-0.48	0.12	90.37	-7.33	**0.000**	**0.000**
	Group X Condition Interaction						
Performance-based variables							
Accuracy	0.09	0.03	0.50	92.78	0.18	0.860	0.882
Reaction Time (s)	0.03	0.02	0.06	78.27	0.47	0.643	0.716
Strategy-based gaze variables							
Exploration	-0.05	-0.05	0.08	93.10	-0.67	0.502	0.606
Vacillations	3.63	0.20	2.14	96.34	1.70	0.093	0.182
Center-Pacman Diff Composite	-7.41	-0.11	3.42	94.25	-2.17	**0.033**	0.075
Center-Pacman Diff First Fixation	-4.70	-0.06	4.04	93.74	-1.16	0.247	0.386
Center-Pacman Diff Fixation	-7.23	-0.11	3.38	94.07	-2.14	**0.035**	0.076
Center-Pacman Diff Fixation Duration	-7.89	-0.12	3.73	94.11	-2.11	**0.037**	0.077
Target-Non-Target Diff Composite	1.63	0.07	2.19	92.28	0.74	0.459	0.579
Target-Non-Target Diff First Fixation	1.26	0.04	3.26	91.85	0.39	0.700	0.758
Target-Non-Target Diff Fixation	1.65	0.07	2.23	92.49	0.74	0.460	0.579
Target-Non-Target Diff Fixation Duration	2.17	0.08	2.23	91.26	0.97	0.334	0.501
Composite z-score							
Global-Local Diff Composite	-0.14	-0.07	0.16	90.58	-0.87	0.385	0.536

Bold $p < .05$; padj reflects the Benjamini-Hochberg correction at a false discovery rate of .10.

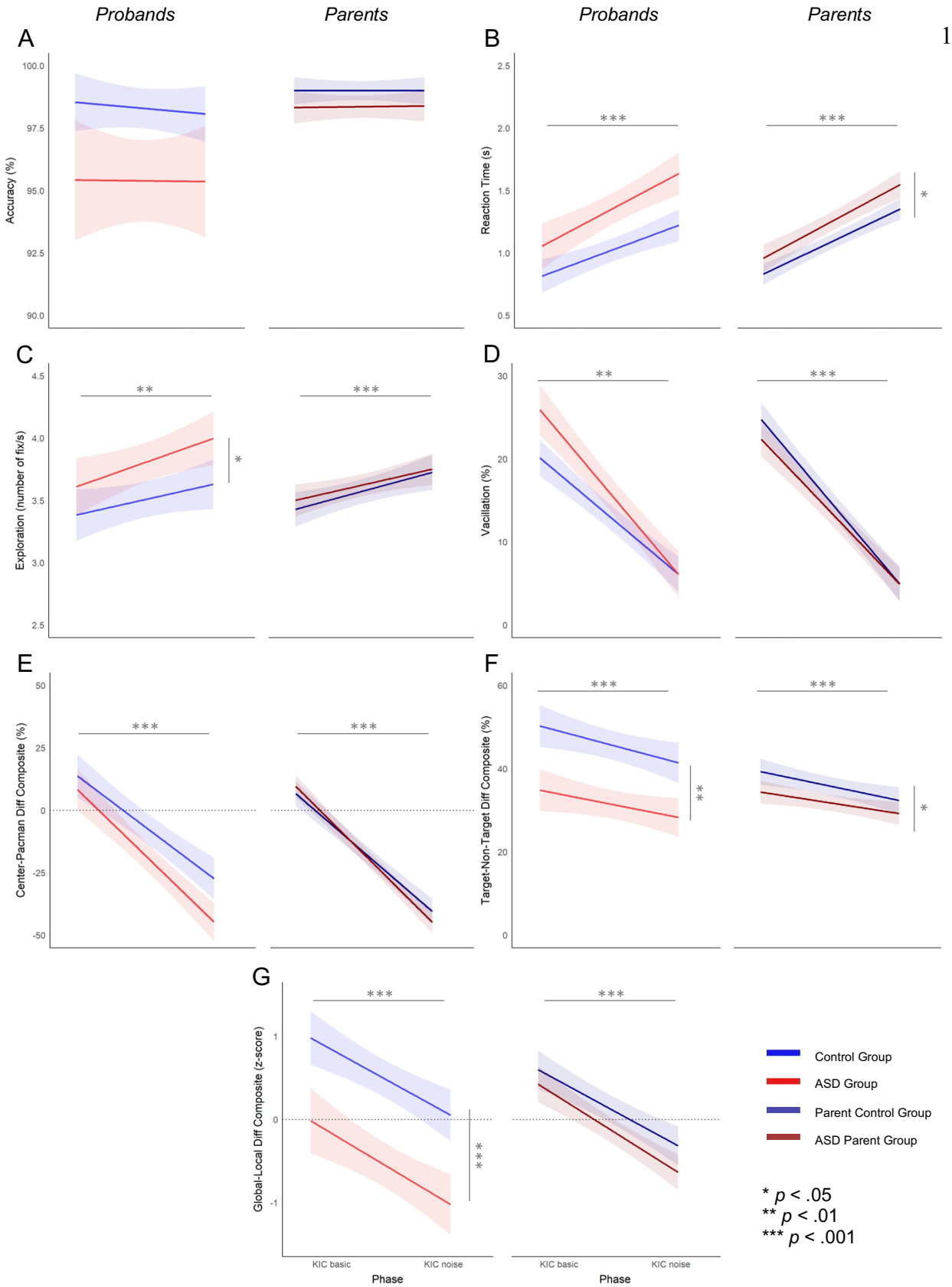

Figure 3.3. *Performance and gaze for the KIC basic and KIC noise condition for A) Accuracy, B) Reaction time, C) Visual exploration, D) Vacillation between target and non-target, E) Center-Pacman composite gaze score, F) Target-NonTarget composite gaze score, G) Global-Local Composite z-score.*

Navon Paradigm (Tables 3.6-3.9; Fig 3.4)

Overall Global-Local Difference Score.

ASD vs. Controls: The ASD group showed a looking profile that was less global than local compared to the control group overall. No groups X condition interaction emerged.

ASD parent vs. parent controls: No main effects of group or group X condition interactions were found.

Performance-based variables

Accuracy.

ASD vs. Controls: Overall, no group differences in accuracy emerged between groups. Non-parametric Mann-Whitney U also revealed no significant group differences in means (control group M_{rank} = 24.20, ASD group M_{rank} = 19.05, U = 166, p = .13).

ASD parent vs. parent controls: Similarly, ASD parent and parent control groups performed similarly on the Navon test, with non-parametric findings also remaining non-significant (parent control group M_{rank} = 45.29, ASD parent group M_{rank} = 42.01, U = 846.5, p = .48).

Reaction Time.

ASD vs. Controls: The ASD and control groups demonstrated comparable reaction times overall as well as when examining letter similarity condition effects. Mann-Whitney U results were also not significant between groups (control group M_{rank} = 20.90, ASD group M_{rank} = 22.05, U = 418, p = .77).

ASD parent vs. parent controls: Similarly, parent groups did not differ overall or when examining differences in performance during *similar* versus *dissimilar* letters. Mann-Whitney U non-parametric tests also revealed no group differences in reaction time overall (parent control group M_{rank} = 43.83, ASD parent group M_{rank} = 43.22, U = 903.5, p = .91).

Strategy-based gaze variables

Exploration.

ASD vs. Controls: No group differences emerged in the number of fixations per second of track time overall, or by letter similarity, with no group X condition interactions emerging.

ASD parent vs. parent controls: Similarly, no overall group or interaction effects emerged.

Percent of Vacillations.

ASD vs. Controls: Overall and across conditions, there were no group differences in the percentage of vacillation between the two Navon options. No interaction effects emerged either.

ASD parent vs. parent controls: Parent groups did not reveal any group or group X condition interaction effects.

Target-NonTarget Difference Score.

ASD vs. Controls: Overall, individuals with ASD demonstrated reduced attention towards the target versus non-target Navon option compared to controls, which was particularly driven by percentage of *fixations* and *fixation duration*. Additionally, a group X condition interaction

showed that the ASD group's target versus non-target looking pattern remained consistent between *similar* versus *dissimilar* letters, while the control group showed greater attention towards the target versus non-target Navon option during *dissimilar* letter trials versus trials with *similar* lettering. This interaction was primarily driven by the percentage of *fixations* towards the target versus non-target option.

ASD parent vs. parent controls: Overall, while no differences emerged for target versus non-target looking, there were group differences in the percentage of first fixations that were made towards the target versus non-target option across conditions. In particular, the ASD parent group showed fewer first fixations towards the target stimulus than the parent control group.

Table 3.6: *Summary of Navon Results - ASD versus control groups.*

	Control Group	**ASD Group**			**Main Effect of Group**		
	M (SD)	M (SD)	*F*	*df*	*p*	*padj*	partial η^2
Performance							
Accuracy^	97.02 (6.85)	75.66 (38.90)	3.81	39	0.058	0.104	0.089
Reaction Time^	2.09 (1.54)	1.95 (1.31)	0.08	39	0.786	0.786	0.002
Gaze Variables							
Exploration	2.89 (0.61)	3.17 (0.58)	2.37	40	0.131	0.168	0.056
Vacillations	25.23 (12.09)	26.84 (9.76)	0.23	40	0.637	0.717	0.006
Target-Non-Target Diff Composite	45.50 (25.32)	24.74 (30.19)	5.76	40	**0.021**	**0.048**	0.126
Target-Non-Target Diff First Fixation	34.65 (27.96)	22.50 (21.07)	2.56	40	0.117	0.168	0.060
Target-Non-Target Diff Fixation	45.01 (23.89)	23.20 (31.59)	6.27	40	**0.016**	**0.048**	0.135
Target-Non-Target Diff Fixation Duration	56.82 (28.04)	28.53 (43.34)	6.17	40	**0.017**	**0.048**	0.134
Composite z-score							
Global-Local Diff Composite	0.25 (1.15)	-0.75 (1.48)	5.90	40	**0.020**	**0.048**	0.129

Bold $p < .05$; padj reflects the Benjamini-Hochberg correction at a false discovery rate of .10; ^IQ added as a covariate

Table 3.7: *Summary of Navon Results - ASD parent versus parent control groups.*

	Parent Control Group	**ASD Parent Group**	**Main Effect of Group**				
	M (SD)	M (SD)	*F*	*df*	*p*	*padj*	partial η^2
Performance							
Accuracy	94.55 (20.30)	89.84 (26.53)	0.83	84	0.366	0.412	0.010
Reaction Time	2.05 (2.35)	1.61 (1.60)	1.08	84	0.301	0.412	0.013
Gaze Variables							
Exploration	3.23 (0.67)	3.48 (0.73)	2.56	84	0.113	0.367	0.030
Vacillations	21.75 (11.68)	22.69 (11.74)	0.14	84	0.710	0.710	0.002
Target-Non-Target Diff Composite	47.90 (23.55)	39.46 (26.45)	2.39	84	0.126	0.367	0.028
Target-Non-Target Diff First Fixation	43.18 (21.36)	31.51 (22.035)	6.15	84	**0.015**	0.136	0.068
Target-Non-Target Diff Fixation	45.10 (24.27)	38.37 (26.77)	1.46	84	0.230	0.412	0.017
Target-Non-Target Diff Fixation Duration	55.41 (29.02)	48.49 (34.65)	0.98	84	0.325	0.412	0.012
Composite z-score							
Global-Local Diff Composite	0.35 (1.17)	-0.05 (1.37)	1.98	84	0.163	0.367	0.023

Bold $p < .05$; padj reflects the Benjamini-Hochberg correction at a false discovery rate of .10

Table 3.8: *Summary of Navon Condition Results- ASD versus Control Groups*

	Control Group		**ASD Group**	
	Navon Dissimilar	**Navon Similar**	**Navon Dissimilar**	**Navon Similar**
	M (SE)	M (SE)	M (SE)	M (SE)
Performance-based variables				
Reaction Time^	1.33 (0.18)	1.36 (0.18)	1.49 (0.17)	1.52 (0.17)
Strategy-based gaze variables				
Exploration	2.88 (0.13)	2.90 (0.14)	3.14 (0.12)	3.19 (0.14)
Vacillations	24.19 (2.98)	26.37 (2.79)	26.67 (2.19)	26.88 (2.39)
Target-Non-Target Diff Composite	51.48 (5.86)	39.94 (6.14)	25.03 (7.25)	24.80 (6.00)
Target-Non-Target Diff First Fixation	50.73 (5.76)	40.03 (5.66)	23.58 (7.43)	23.42 (6.40)
Target-Non-Target Diff Fixation	60.76 (6.58)	53.55 (6.41)	28.5 (10.13)	29.15 (8.61)
Target-Non-Target Diff Fixation Duration	42.94 (6.22)	26.25 (7.45)	23.02 (5.46)	21.83 (5.16)
Composite score				
Global-Local Diff Composite	0.47 (0.30)	-0.06 (1.39)	-0.82 (0.35)	-0.86 (0.30)

ASD versus control groups	*Estimate*	β	*SE*	*df*	*t value*	*p*	*padj*
			Main Effect of Condition				
Performance-based variables							
Reaction Time^	0.04	0.00	0.03	40.00	1.19	0.240	0.350
Strategy-based gaze variables							
Exploration	0.02	0.02	0.07	40.00	0.31	0.761	0.802
Vacillations	2.18	0.09	1.94	40.00	1.12	0.268	0.358
Target-Non-Target Diff Composite	-11.53	-0.19	3.82	40.00	-3.02	**0.004**	**0.024**
Target-Non-Target Diff First Fixation	-16.69	-0.29	5.92	40.00	-2.82	**0.007**	**0.030**
Target-Non-Target Diff Fixation	-10.70	-0.17	3.54	40.00	-3.03	**0.004**	**0.024**
Target-Non-Target Diff Fixation Duration	-7.21	-0.09	3.61	40.00	-2.00	*0.053*	0.106

Composite score							
Global-Local Diff Composite	-0.53	-0.17	0.18	40.00	-3.02	**0.004**	**0.024**
	Group X Condition Interaction						
Performance-based variables							
Reaction Time^	-0.01	0.00	0.04	40.00	-0.25	0.802	0.802
Strategy-based gaze variables							
Exploration	0.03	0.02	0.09	40.00	0.35	0.728	0.802
Vacillations	-1.98	-0.08	2.69	40.00	-0.74	0.466	0.573
Target-Non-Target Diff Composite	11.30	0.16	5.28	40.00	2.14	**0.039**	0.103
Target-Non-Target Diff First Fixation	15.49	0.24	8.18	40.00	1.89	*0.066*	0.117
Target-Non-Target Diff Fixation	10.54	0.15	4.88	40.00	2.16	**0.037**	0.103
Target-Non-Target Diff Fixation Duration	7.86	0.09	4.99	40.00	1.57	0.123	0.197
Composite score							
Global-Local Diff Composite	0.48	0.14	0.24	40.00	1.99	*0.053*	0.106

Bold $p < .05$; padj reflects the Benjamini-Hochberg correction at a false discovery rate of .10; ^IQ added as a covariate

Table 3.9: *Summary of Navon Condition Results - ASD Parent versus Parent Control Groups*

	Parent Control Group		**ASD Parent Group**	
	Navon Dissimilar	**Navon Similar**	**Navon Dissimilar**	**Navon Similar**
	M (SE)	M (SE)	M (SE)	M (SE)
Performance-based variables				
Reaction Time	1.01 (0.04)	1.01 (0.03)	1.08 (0.03)	1.13 (0.04)
Strategy-based gaze variables				
Exploration	3.20 (0.11)	3.24 (0.12)	3.45 (0.11)	3.49 (0.11)
Vacillations	19.61 (2.00)	23.84 (2.00)	22.26 (1.88)	23.07 (1.74)
Target-Non-Target Diff Composite	52.08 (3.97)	43.96 (3.92)	42.5 (4.00)	36.61 (4.03)
Target-Non-Target Diff First Fixation	49.02 (4.07)	41.71 (4.05)	41.06 (4.00)	36.10 (4.13)
Target-Non-Target Diff Fixation	58.68 (4.84)	52.39 (4.71)	51.29 (5.16)	46.00 (5.15)
Target-Non-Target Diff Fixation Duration	48.55 (3.76)	37.78 (3.93)	35.15 (3.5)	27.72 (3.73)
Composite score				
Global-Local Diff Composite	0.63 (0.19)	0.21 (0.19)	.10 (0.20)	-0.19 (0.19)

ASD parent versus parent control groups	*Estimate*	β	*SE*	*df*	*t value*	*p*	*padj*
			Main Effect of Condition				
Performance-based variables							
Reaction Time	0.01	-0.01	0.03	84.00	0.21	0.837	0.893
Strategy-based gaze variables							
Exploration	0.04	0.02	0.06	84.00	0.54	0.590	0.726
Vacillations	4.24	0.17	1.36	84.00	3.12	**0.002**	**0.010**
Target-Non-Target Diff Composite	-8.12	-0.15	2.34	84.00	-3.47	**0.001**	**0.007**
Target-Non-Target Diff First Fixation	-10.77	-0.21	3.54	84.00	-3.04	**0.003**	**0.010**
Target-Non-Target Diff Fixation	-7.30	-0.14	2.37	84.00	-3.08	**0.003**	**0.010**

Target-Non-Target Diff Fixation Duration	-6.29	-0.10	2.18	84.00	-2.88	**0.005**	**0.013**
Composite score							
Global-Local Diff Composite	-0.41	-0.16	0.11	84.00	-3.73	< 0.0001	**0.006**
	Group X Condition Interaction						
Performance-based variables							
Reaction Time	0.05	0.08	0.04	84.00	1.33	0.186	0.372
Strategy-based gaze variables							
Exploration	0.01	0.01	0.09	84.00	0.14	0.893	0.893
Vacillations	-3.43	-0.12	1.84	84.00	-1.87	*0.065*	0.149
Target-Non-Target Diff Composite	2.23	0.04	3.17	84.00	0.70	0.483	0.649
Target-Non-Target Diff First Fixation	3.35	0.06	4.79	84.00	0.70	0.487	0.649
Target-Non-Target Diff Fixation	2.34	0.04	3.21	84.00	0.73	0.467	0.649
Target-Non-Target Diff Fixation Duration	1.00	0.01	2.95	84.00	0.34	0.736	0.842
Composite score							
Global-Local Diff Composite	0.12	0.04	0.15	84.00	0.80	0.427	0.649

Bold p < .05; padj reflects the Benjamini-Hochberg correction at a false discovery rate of .10

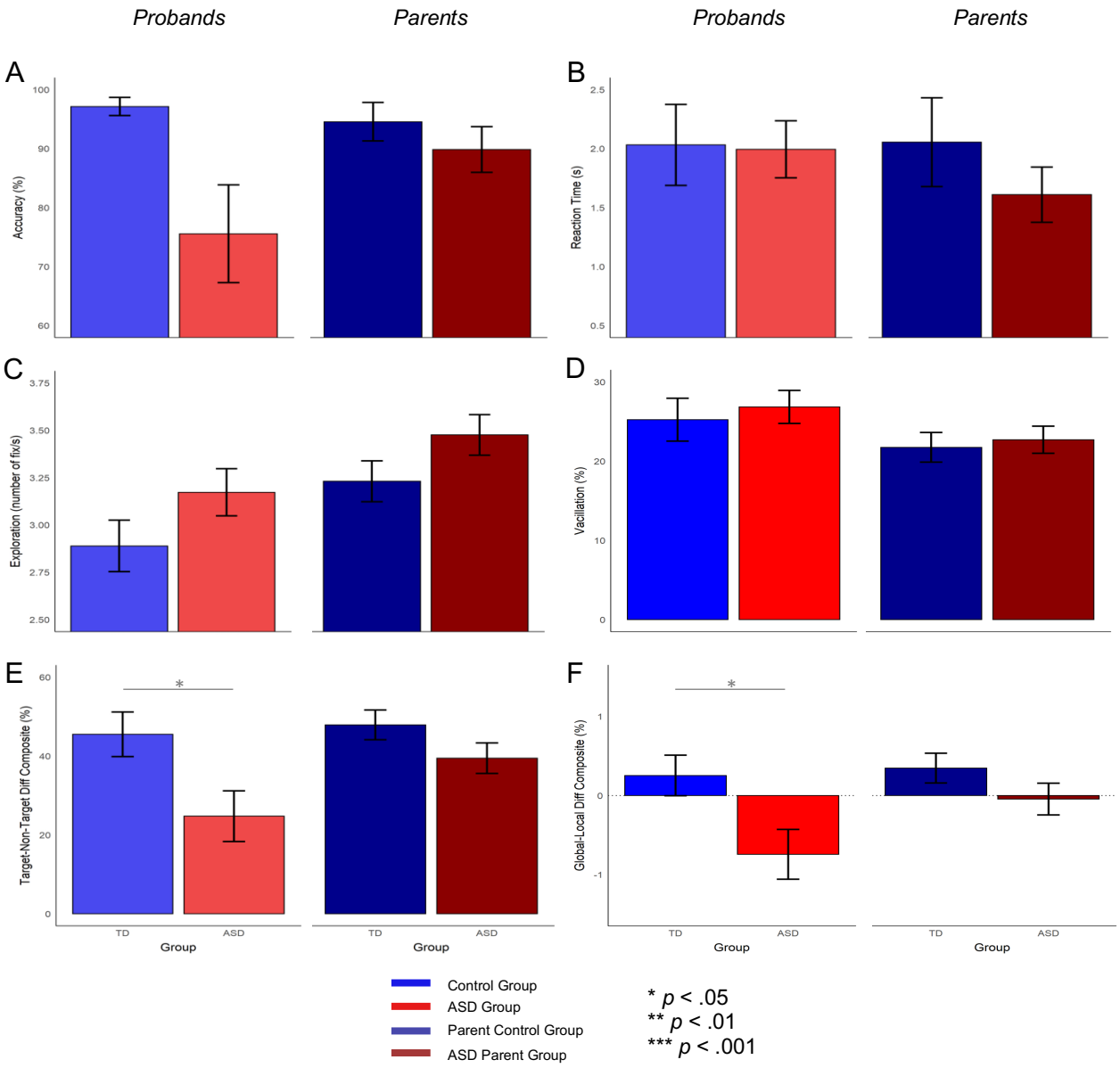

Figure 3.4. *Group differences for the Navon Paradigm overall for A) Accuracy, B) Reaction time, C) Visual exploration, D) Vacillation between target and non-target, E) Target-NonTarget composite gaze score, F) Global-Local Composite z-score*

Across Local/Global Perception Tasks (Tables 3.10 - 3.11; Figs. 3.5)

Target-NonTarget Difference Score.

ASD vs. Controls: The ASD group demonstrated significantly reduced attention towards the target versus non-target option compared to the control group.

ASD parent vs. parent controls: Parents showed no overall group differences in attention towards the target versus non-target option.

Overall Global-Local Difference z-score.

ASD vs. Controls: Group differences emerged showing that control groups demonstrated greater global versus local processing compared to the ASD group across tasks.

ASD parent vs. parent controls: Parent groups demonstrated comparable global versus local processing styles, though patterns trended in the same direction as proband group differences.

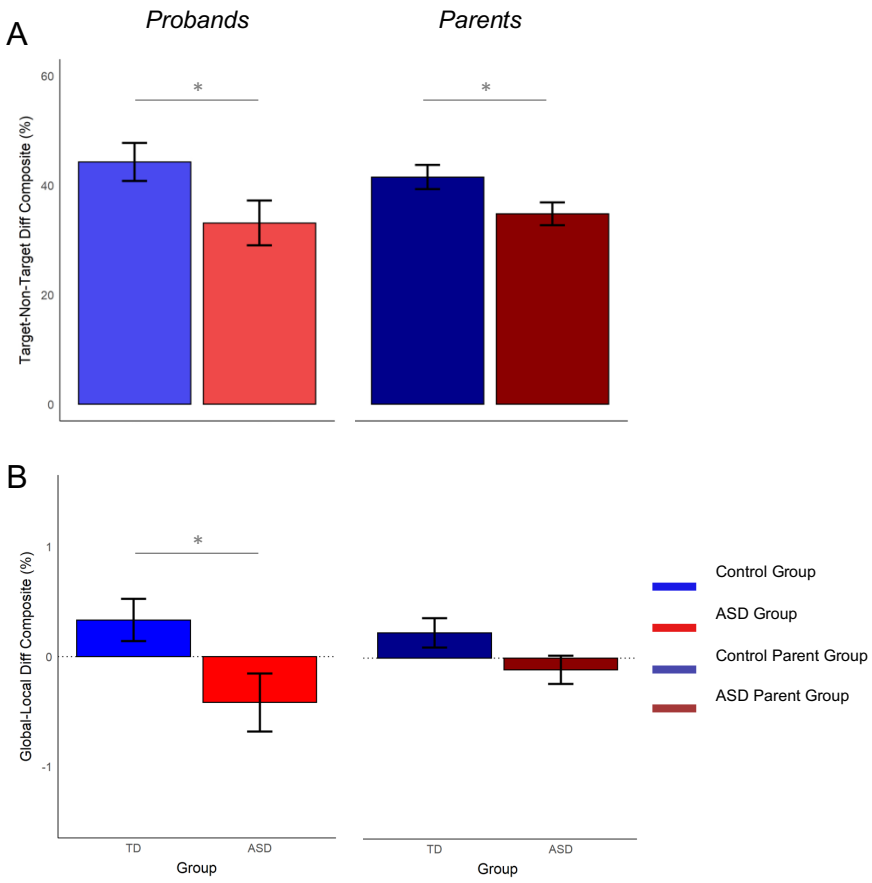

Figure 3.5. *Group differences across tasks indicate A) ASD and ASD parents looked more comparably to target and non target stimuli than control counterparts, who looked more to target stimuli and B) Overall, the ASD group processed more locally than their TD counterparts (more global) with a similar but nonsignificant pattern emerging for parent groups.*

Table 3.10: *Summary of cross-task Results - ASD versus control groups.*

	Control Group	**ASD Group**		**Main Effect of Group**			
	M (SD)	M (SD)	*F*	*df*	*p*	*padj*	partial η^2
Gaze Variables							
Target-Non-Target Diff Composite	44.27(15.08)	33.11 (15.87)	4.38	32	**0.044**	**0.044**	0.120
Composite z-score							
Global-Local Diff Composite	0.33 (0.84)	-0.42 (1.03)	5.50	32	**0.025**	**0.044**	0.147

Bold $p < .05$; padj reflects the Benjamini-Hochberg correction at a false discovery rate of .10

Table 3.11: *Summary of cross-task Results - ASD parent versus parent control groups.*

	Parent Control Group	**ASD Parent Group**		**Main Effect of Group**			
	M (SD)	M (SD)	*F*	*df*	*p*	*padj*	partial η^2
Gaze Variables							
Target-Non-Target Diff Composite	41.51 (13.69)	34.79 (13.87)	4.84	80	**0.031**	**0.061**	0.057
Composite z-score							
Global-Local Diff Composite	0.23 (0.82)	-0.11 (0.85)	3.27	80	0.074	0.074	0.039

Bold $p < .05$; padj reflects the Benjamini-Hochberg correction at a false discovery rate of .10

Association between Performance and Gaze Variables (*Fig.* 3.6)

ASD and Controls. With groups combined, a significant correlation emerged between the *Target-NonTarget Difference Score* and accuracy for KIC and Navon tasks ($r = .44$, $p < .01$ and $r = .67$, $p < .0001$) and reaction time for KIC only ($r = -.64$, $p < .0001$), demonstrating that the more accurate and quicker participants were in responding, the more they attended towards the target (versus non-target) KIC or Navon option. Similarly, the faster and more accurate participants performed, the less often they vacillated between the two KIC options ($r = .59$, $p < .0001$ and $r = -.47$, $p = .001$, respectively). Only accuracy significantly correlated with percent vacillations ($r = -.33$, $p < .05$) for the Navon Paradigm, showing fewer vacillations and greater target (versus non-target) looking relating to higher accuracy. For the KIC paradigm, reaction time was significantly negatively associated with *Center-Pacman Difference Score* ($r = -.33$, $p < .05$) representing faster response times when there was greater attention directed to the KIC centers (versus Pacman). No associations with accuracy or reaction time with exploration were found in either task. Finally, higher accuracy and quicker response times were significantly correlated with one another for both KIC and Navon tasks ($r = -.54$, $p < .0001$ and $r = -.38$, $p < .05$, respectively). All significant and non-significant associations remained consistent upon re-analysis using non-parametric Spearman tests.

ASD parent and parent controls. For parents (both ASD parent and parent control groups combined), a significant correlation between accuracy, reaction time and *Target-NonTarget Difference Score* during KIC revealed that the more parents attended to the target, the higher their accuracy ($r = .34$, $p = .001$) and the quicker their response times ($r = -.56$, $p < .0001$). Only accuracy was significantly correlated with *Target-NonTarget Difference Score* in the Navon paradigm ($r = -.22$, $p < .05$) (though, Spearman correlations revealed significant positive and negative relationships for accuracy and reaction time, respectively; rs $> |.35|$, ps $< .001$). A positive correlation also emerged between reaction time and vacillations ($r = .25$, $p < .05$) for the KIC paradigm (and for the Navon

paradigm with Spearman tests; $r = .23$, $p < .05$), indicating slower response times when participants vacillated more between the two target/no-target options. Similarly, no associations with reaction time and exploration were found in either task, though, a positive correlation in the Navon task demonstrated elevated exploration rates relating to reduced accuracy ($r = -.22$, $p < .05$). Finally, a negative correlation emerged between reaction time and accuracy for the KIC ($r = -.24$, $p < .05$), but not for the Navon paradigm. Similar to the proband groups, Spearman correlation results remained largely consistent with Pearson results reported here.

3. Parent-Child Associations Across Tasks (*Fig. 3.7*)

ASD families.

Significant parent-child associations emerged such that increased global looking patterns in parents predicted 34% of the variance of increased global looking patterns in their children (*estimate* = .62, *SE* = .27, $t = 2.26$, $p < .05$). In terms of the permutation test, *Pearson's* correlations for global versus local looking was significant for ASD families ($r = .60$, $p < .05$), with a 97.3% likelihood that the correlation coefficient derived from the true parent-child dyad correlation (r_{true}) is greater than the correlation coefficients derived from all permutations of the unrelated parent-child pairs (r_{random}) (i.e., probability $r_{true} > r_{random} = 97.3\%$).

Control families

<u>*Parent-child pairs*</u>. No significant parent-child associations emerged in the *Overall Global-Local Difference Score* composite for control families, with only 1.4% of variance in child global looking being explained by that of their parents (*estimate* = .15, *SE* = .30, $t = .49$, $p = .63$). The permutation test revealed non-significant *Pearson's* correlations for global versus local looking for control families ($r = .18$, $p = .45$), with a 76.2% likelihood that the correlation coefficient derived

from the true parent-child dyad correlation is greater than the correlation coefficients derived from all permutations of the unrelated parent-child pairs (i.e., probability $r_{true} > r_{random} = 76.2\%$).

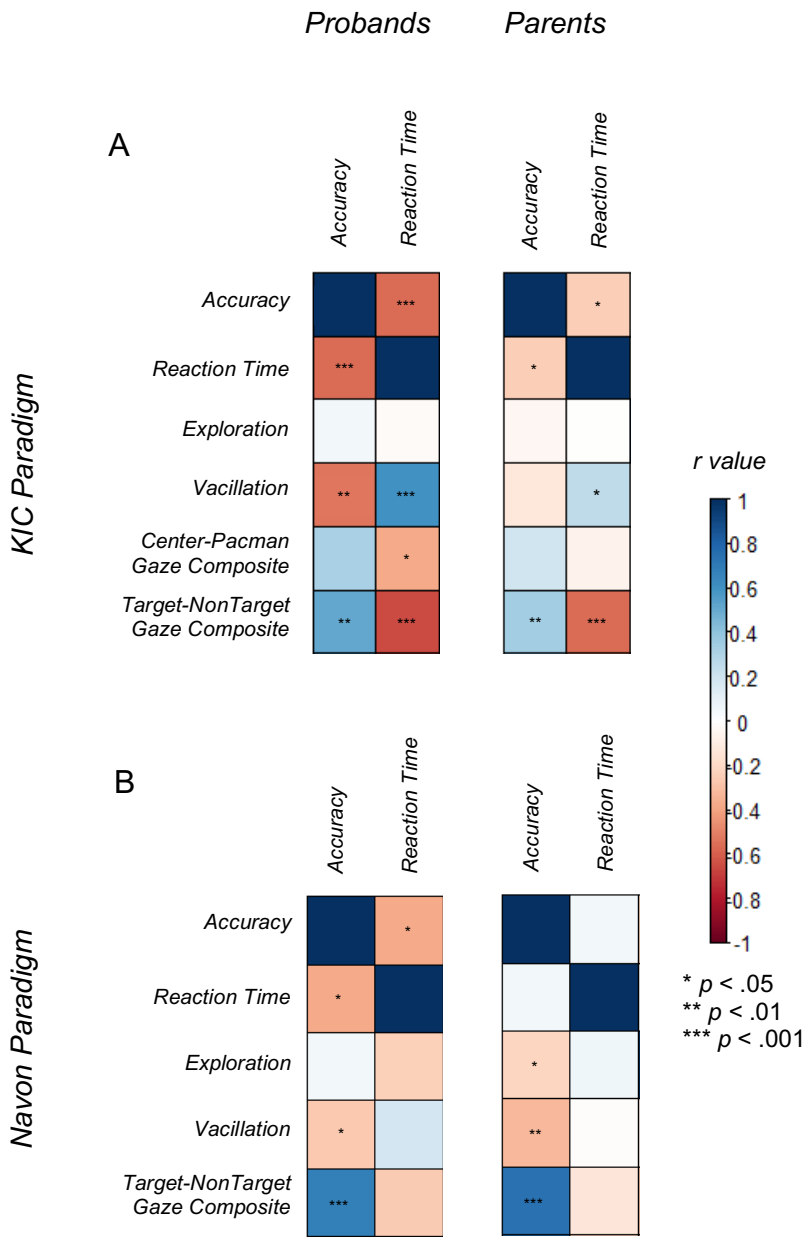

Figure 3.6. *Grids depict inter-variable correlations for A) the KIC Paradigm (KIC basic and KIC noise combined), and B) the Navon Paradigm between performance indices (accuracy and reaction time) and gaze variables.*

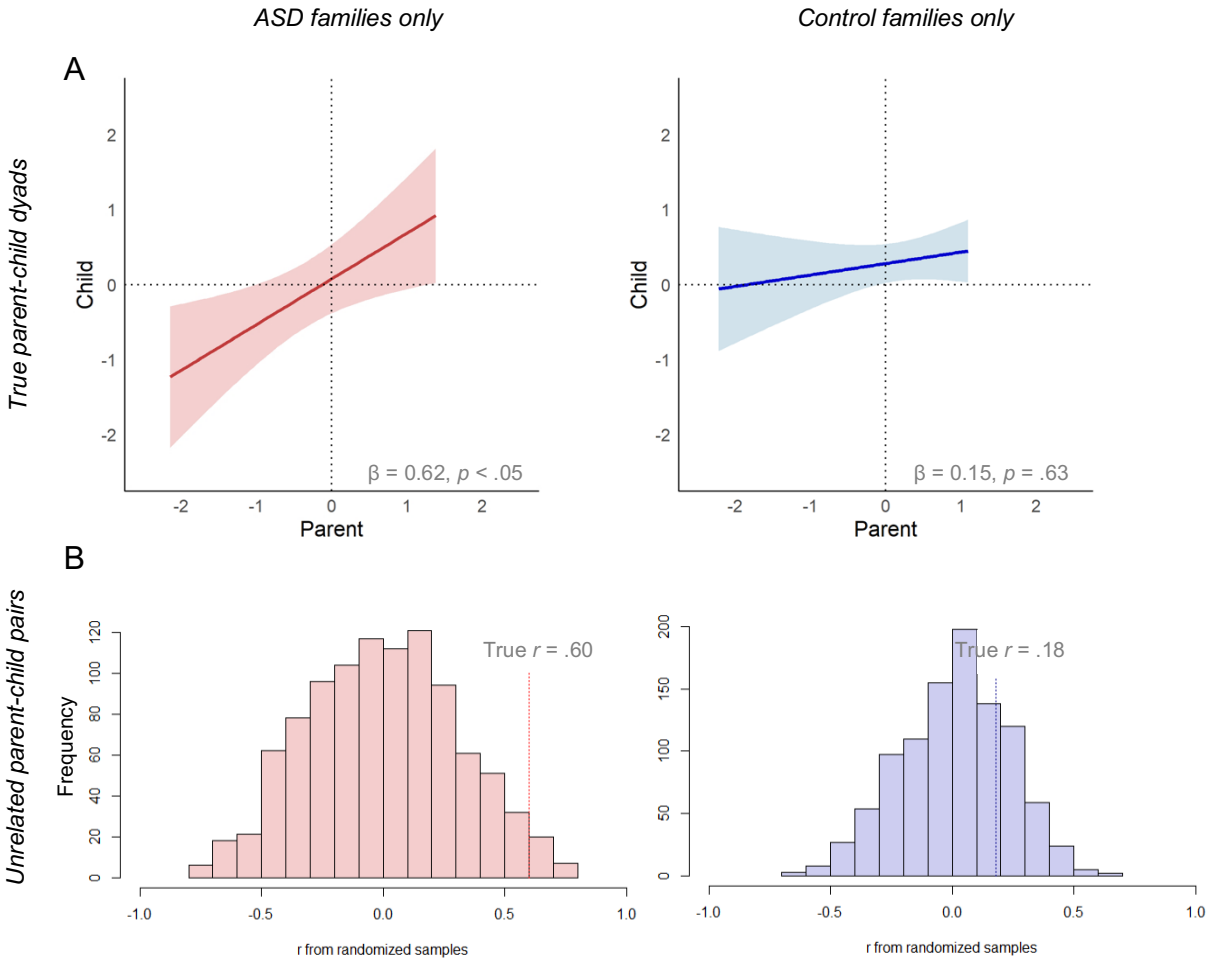

Figure 3.7. *Parent child correlations in the Overall Global-Local Difference z-score. A) Correlations for matched pairs of parents and their children indicate a moderate-strong relationship of gaze patterns in ASD families only. B) This effect is not seen in ASD or Control families when a child is paired with a different parent in the respective parent group. Distributions produced from randomization test to examine familiality of local/global processing in parent and child dyads. Frequency distribution reflects the frequency of obtaining a correlation coefficient value for random parent-child pairings; arrow signifies true correlation coefficient between parent and child dyad. For ASD families, probability* $r_{true} > r_{random} = 97.3\%$*; for Control families, probability* $r_{true} > r_{random} = 76.2\%$.

4. Relationship with Clinical-Behavioral Correlates Across Tasks (Fig. 3.8)

Probands.

Clinical-Behavioral Correlates. Negative associations between reaction time and RBS-R total score emerged, indicating slower response speeds correlating with greater rates of RRBs as measured by the RBS-R ($r = .79$, $p < .05$). Similarly, increased fixation rate and vacillation significantly positively correlated with greater rates of RRBs based on the ADI current scores ($r = .71$, $p < .05$ and $r = .85$, $p < .01$, respectively) (*Figs*. 3.8A and B). No associations between ADOS severity scores or SRS emerged among individuals with ASD. In the ASD group, significant positive associations between the *global-local difference composite z-score* and greater pragmatic language violations, particularly in speech and language behaviors (e.g., being formal, scripting) and theory of mind-related behaviors emerged (e.g., failing to clarify or to provide background information) ($r = .70$, $p < .01$ and $r = .61$, $p < .05$, respectively) (*Fig*. 3.8C). Significant correlations emerged for the control group with increased pragmatic language abilities and higher accuracy ($r = -.55$, $p < .05$).

Cognitive Correlates. No associations were found between local/global variables and social cognition or measures of executive function (age-corrected standard score on the Flanker task; GEC T-score from the BRIEF questionnaire) in either group.

Parents.

Clinical-Behavioral Correlates. No significant correlations emerged with measures of the broad autism phenotype, but a positive correlation of medium effect emerged between the *global/local composite z-score* with the PRS total score in the ASD parent group. Additionally, in parents of individuals with ASD, a negative correlation between number of vacillations emerged with the PRS total score, indicating that greater pragmatic language violations occured with greater global versus local processing ($r = .34$, $p < .05$ and $r = -.32$, $p < .05$). Specifically, among parents of

individuals with ASD, the socially withdrawn factor score (which includes items such as being unable to clarify, failing to elaborate, failing to reciprocate) was related to greater global versus local processing (r = .34, p < .05) (*Fig.* 3.8D), greater rates of vacillations (r = -.36, p < .05), and greater target versus non-target attention (r = .34, p < .05). No significant associations with pragmatic language and local/global variables emerged in the parent control group.

Cognitive Correlates. No significant correlations emerged with The Eyes Test or either executive funcioning measure, for ASD parent or control groups.

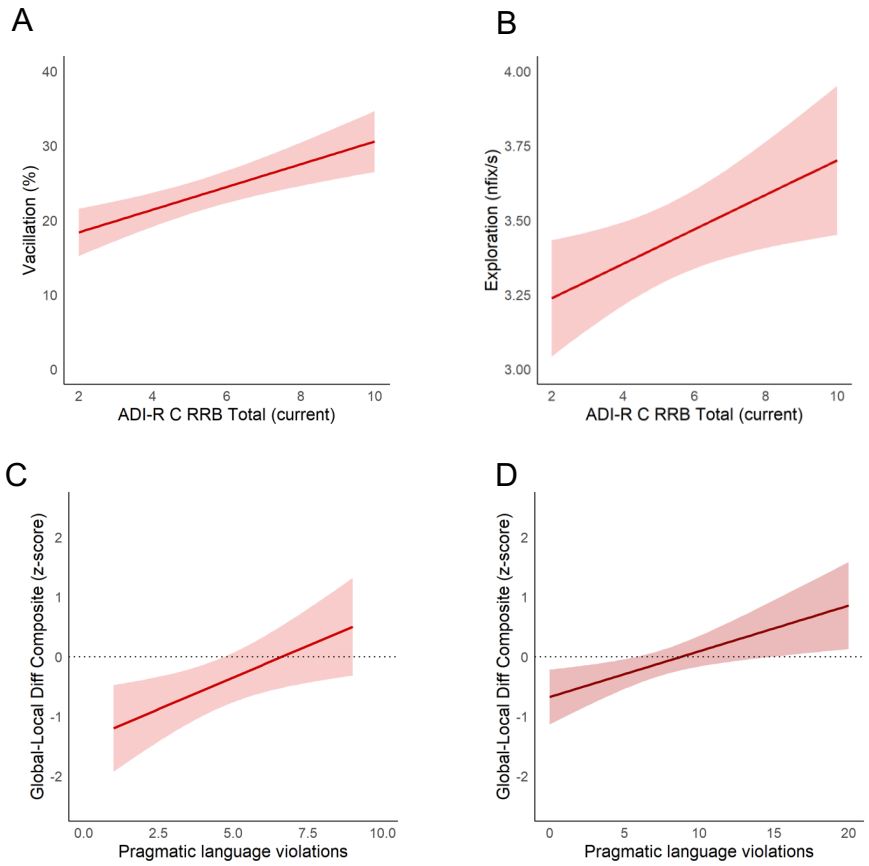

Figure 3.8. *Clinical-behavioral correlates or local/global processing. A) and B) depict significant associations between elevated rates of restricted and repetitive behaviors (RRB) based on the Autism Diagnostic Interview-Revised (ADI-R) with increased vacillation and exploration across tasks; C) individuals with ASD and D) parents of individuals with ASD show greater global processing abilities relating to poorer pragmatic language abilities (higher score = greater impairment).*

Discussion

Using a suite of eye-tracking indices applied to two tasks tapping local and global perception, this study examined visual processing styles among individuals with ASD and their parents. Specifically, this study aimed to replicate and expand upon prior work showing differences in local/global processing using Kanizsa Illusory Contours (KICs; an illusory shape induced by strategically placed pacman elements) and Navon Hierarchical figures, in a sample of adolescents and adults with ASD. This study also uniquely investigated such processes among parents of individuals with ASD. Findings demonstrated robust differences between individuals with ASD versus controls, with subtle, and nuanced differences emerging among parent groups within and across tasks. Within family similarities of processing styles emerged primarily for ASD parent-child pairs, but not for control parent-child pairs. Finally, there were links between visual processing styles and ASD-related symptomatology, as evidenced by relationships with elevated rates of restricted and repetitive behaviors in individuals with ASD and better pragmatic (i.e., social) language in both ASD proband and parent groups. Associations suggest that local/global visual processing profiles may differentially impact broader clinical and subclinical traits related to ASD. Together, eye-tracking findings potentially indicate that visual processing styles may be familial, genetically meaningful features of the broad autism spectrum, thereby underscoring their utility as a candidate endophenotype and contributing to our understanding of potential underlying mechanisms of the broad autism phenotype (BAP).

Performance in ASD versus controls

Non-parametric results revealed that the ASD groups tended to be less accurate and slower to respond than the control group across conditions in the KIC task. Findings are similar to prior work in school-age children that demonstrated significant (but minimal) accuracy and reaction time

differences during the more complex KIC noise condition, which included local interference (Nayar et al., 2017). Importantly, however, all individuals responded with 78% or greater accuracy, suggesting relatively intact performance across groups. Prior work using performance measures have similarly demonstrated adult-like global perception in adult controls (Nayar et al., 2015) and a reduced *preference* with no impairment in global processing among adults with ASD (Koldewyn et al., 2013). In contrast, it appears that performance on these tasks may be impacted by age (7-13 years in Nayar et al., 2017 and 9-32 in the current study), with clearer reduced global processing observed in studies with younger samples. Although preliminary analyses showed no significant correlations with age in the current sample, it remains possible that a protracted developmental process of global perception resulting from ASD manifests in a "rightward shift" in developmental trajectories in task performance relative to controls (Nayar et al., 2015), slowing the development of global perception even further in ASD. Finally, quicker reaction times related to increased accuracy and greater global perception based on gaze variables in ASD and controls, and slower response speeds related to reduced global perception (i.e., greater vacillations between options, and fewer target/global looks in the KIC task) in the present study. Such findings are consistent with original landmark findings from studies involving Navon Hierarchical Figures suggesting that global processing strategies are quicker and more efficient than effortful local perceptual processes (Navon, 1977) based on performance measures alone.

Gaze in ASD versus controls during KIC paradigm

There is some debate on whether individuals with ASD exhibit heightened local processing in the absence or presence of impaired global processing (Simmons & Todorova, 2018; Van der Hallen et al., 2015). Newly uncovered patterns in the present study in the ASD group showing increased visual exploration and vacillation relative to controls in both the KIC and Navon tasks, which are

indicative of heightened local perception (alongside reduced global perception). Greater vacillation between stimuli generally represents a less mature visual processing style. They also point to greater levels of uncertainty, which has been shown to be particularly characteristic of younger children engaging in the processes of comparison or elimination before adult-like global processing comes online (Nayar et al., 2015). Greater vacillations suggests that individuals with ASD may be less readily able to appreciate the global form, and were therefore more likely to rely on a comparative strategy (between the target and non-target) than controls. This type of processing style is also consistent with the idea of slower or delayed global processing. For instance, Van Der Hallen and colleagues' (2015) meta-analysis of studies investigating local and global perception concluded that despite an overall reduced global preference, cross-study findings were heavily reliant on the speed at which different visual processing strategies unfold. In particular, the analysis highlights the tendency for individuals with ASD to attend initially to information at the local level, shifting towards global processing strategies with prolonged looking. This tendency became more apparent in tasks with greater local interference (such as the KIC noise condition in the present study) (also see Nayar et al., 2017), such as the embedded figures test and the Rey-Osterrieth Complex Figure.

Additionally, individuals with ASD tended to make a greater number of fixations per second, representing greater exploration rates compared to controls, indicative of increased levels of detailed processing. While not being assessed from a local/global processing framework, existing findings mirror prior reports detailing elevated rates of exploration and perseverative or refixations (i.e., repeat fixations) among individuals with ASD, particularly towards both social and non-social, high-interest images during a passive-viewing task (Sasson et al., 2008). Similarly, Nayar et al., (2018) demonstrated elevated rates of refixations during a non-social language processing task; a pattern also evident among parents of individuals with ASD exhibiting BAP traits. Findings of increased exploration or refixations across non-social tasks (the present study), social information and non-

social images (Sasson et al., 2008; Swanson et al., 2013), scenes (Au-Yeung et al., 2011), and a language processing task (Nayar et al., 2018), highlights the utility of perseverative or detailed fixation patterns as a stable, cross-context biomarker for ASD. That increased vacillations and exploration related to increased rates of restricted and repetitive behaviors (RRBs) in ASD in the current study, further suggests their specificity to traits inherent to ASD and may potentially represent an underlying biological mechanism related to RRBs.

Findings from eye-tracking in this study have strong implications for our understanding of clinical and sub-clinical traits related to the weak central theory account in ASD. In KICs, the global form can be appreciated by integrating the local pacman elements to generate the coherent whole shape — this process is particularly automatized and occurs within the first 300 ms of perception according to studies examining neural responses to KICs (Foxe et al., 2005). In other words, there is evidence of a "pop out" effect, and prior work has suggested that attending to the center of the KIC indicates greater global perception, whereas looking to individual pacman elements reflects more detailed processing styles (Guttman & Kellman, 2004; Ringach & Shapley, 1996). In the current study, the difference between looks to center and pacman was examined for the KIC task only. While overall group differences between individuals with ASD and controls were reported in (Nayar et al., 2017), the current study yielded robust group by condition effects among probands. During the KIC basic condition, both groups exhibited greater fixations to center than pacman (as indicated by the positive values) and did not differ from one another. In contrast, during the condition with local interference (i.e., KIC noise condition), the ASD group showed a pattern of looking that reflected heightened local processing compared to controls, though both groups generally attended to pacman features more than the KIC centers (as indicated by the negative values). During this more complex task, participants were required not only to integrate (i.e., fill in the illusion) but also to segregate (i.e., extract the relevant pacman elements for integration for both the target and non-target KICs),

suggesting a higher level of perceptual and attentional demands posed by the KIC noise condition. Additionally, findings of decreased target relative to non-target fixations during this KIC noise condition across groups, highlights the dual processing (i.e., integration and segregation) nature required for success during the complex KIC noise condition. Importantly, this effect was amplified for those with ASD, which suggests that individuals with ASD may be utilizing a developmentally immature strategy (Nayar et al., 2015) relative to controls.

Together, findings demonstrate that individuals with ASD likely employ heightened local processing strategies (i.e., increased vacillations and exploration) coupled with reduced global processing strategies (i.e., decreased center and target fixations), in the relative absence of global impairments (i.e., no significant differences in accuracy or reaction time). These findings are consistent with studies documenting the ability of individuals with ASD to shift to global processing when required to do so (particularly in studies employing the Navon Hierarchical Figures) (Koldewyn et al., 2013; Mottron et al., 2003; Mottron et al., 1999; Neufeld et al., 2020; Van der Hallen et al., 2015), suggesting that the weak central coherence (Happe & Frith, 2006), local processing bias (Frith & Happe, 1994; Kanner, 1943; Pellicano & Burr, 2012), or the enhanced local-processing efficiency (Bertone et al., 2005; F. Happe, 1996; Jolliffe & Baron-Cohen, 1997; Joseph et al., 2009; Kemner et al., 2008; Minshew et al., 1997; O'Riordan & Plaisted, 2001; Shah & Frith, 1983, 1993) theories hold true for the present study. As such, findings from this study contribute to the historical debate surrounding local and global processing in ASD, as this study not only utilizes two well-established paradigms of local/global processing with defined neural substrates for the KIC stimuli in particular, but also help address the *strategies* being employed to better extrapolate local/global processing styles.

<u>Gaze in ASD versus controls during the Navon paradigm</u>

A wealth of research documents key differences between controls and ASD exist using the Navon stimulus (Koldewyn et al., 2013; Mottron et al., 2003; Mottron et al., 1999; Van der Hallen et al., 2015; Van Eylen et al., 2017; Van Eylen et al., 2018). Surprisingly, in contrast to these prior findings, no group differences in vacillations and exploration were observed in the Navon paradigm. Given that this task was specifically designed to assess preference for local or global options, with a global cue (i.e., the real sample letter), fewer group differences for Navon suggest that individuals with ASD are able to engage in global processing adequately when cued, and that differences emerging in the KIC task represent greater perceptual differences in visual strategies. Prior work using Navon stimuli has demonstrated that when individuals with ASD are primed or instructed to utilize global perception, they are able to efficiently do so (Koldewyn et al., 2013; Neufeld et al., 2020; Plaisted et al., 1999). Our findings in Navon, however, additionally imply that they may be utilizing a different strategy to engage in global processing. In particular, it appears that individuals with ASD exhibit greater target versus non-target fixations, despite a lack of difference in vacillations between the target and non-target figures. This suggests that perceptual strategies may differ between groups, despite similarities in performance-based measures.

A group by condition interaction for target fixations further suggests the impact of similar versus dissimilar letters on efficient global processing despite the presence of a global cue and the lack of differences in performance measures. Prior work has indicated that even typically developing individuals and high functioning individuals with ASD demonstrate slower response times when letters are morphologically similar (e.g., B and P) versus dissimilar (e.g., H and X) (Lamb & Robertson, 1989; Mottron et al., 1999). In the present study, those with ASD appeared to exhibit greater interference than controls during the morphologically similar versus dissimilar letter trials, evidenced by fewer target versus non-target fixations when letters were similar. Differences between

KIC and Navon tasks presented in this study, as well as key effects emerging from letter similarity can help to inform future local and global perception studies using Navon hierarchical figures.

Performance and gaze in ASD parents versus parent controls

Parent findings revealed differences in reaction time in the KIC paradigm. Specifically, parents of individuals with ASD responded more slowly than controls (although, all groups tended to respond within 1 second) and non-parametric tests showed relatively reduced accuracy among ASD parents as well. Similar to proband groups and consistent with prior literature, faster reactions times also related to increased accuracy and greater overall global perception across groups, highlighting the benefits of speed and accuracy of global perception.

In terms of eye-tracking results, while parent groups did not demonstrate increased rates of vacillations and exploration across and within tasks, both groups did show greater exploration relating to reduced accuracy in the Navon task. Given that vacillation and exploration are indicative of heightened local perceptual strategies, comparable rates of exploring or vacillating in parents point to the absence of heightened local processing. These findings contradict much of the literature demonstrating elevated levels of detail orientation among parents of individuals with ASD probed via questionnaires about daily life (Hurley et al., 2007; Van Eylen et al., 2017), described during semi-structured conversations (Losh, 2011; Piven, Palmer, Landa, et al., 1997), and evidenced by eye movements during a language processing task (Nayar et al., 2018). Differences between the present study and the previous literature is the primary focus on low-level visual perceptual deficits over higher level processes such as language and personality traits, as well as self-perceptions of general detail orientation in everyday life. Given that parents generally do not present with clinical diagnoses of ASD, lack of heightened local processing in the context of a local/global visual perception-based task is not unsurprising (Losh et al., 2009), where heightened local processing was not observed in a

task of block design. As such, heightened local processing as observed in ASD may not necessarily be a promising measurable endophenotype according to the examination of vacillations and exploration variables from tasks included in the present study.

On the other hand, parents of individuals with ASD demonstrated a reduced propensity for employing global perceptual strategies, in the absence of difference in local processing. In particular, they too showed diminished target versus non-target looks compared to parent controls, and reduced center versus pacman fixations during the KIC noise condition with local interference, complementing results observed in proband groups. As such, it appears that parents' global processing is not impaired (given highly accurate responding) but is similarly reduced in the presence of local distractors, and they may thus rely on different strategies to complete the task compared to parent controls. Interestingly, differences observed in the Navon task were subtle and nuanced—specifically, parents of individuals with ASD made fewer first fixations towards the target (i.e., global match) versus the non-target (i.e., local match), compared to parent controls. It may be that parent controls are able to tap peripheral visual processes to engage in greater global processing, which reflects faster and more efficient processing more broadly (Kimchi, 1992; Nayar et al., 2015). In contrast, parents of individuals with ASD may be less efficient at capitalizing peripheral visual strategies to engage in this task. Indeed, prior work has suggested that global processing has greater precedence in the periphery, and perhaps ASD parents are less efficient at attending to peripheral stimuli than parent controls (Kimchi, 1992). Given known differences in social orientation in ASD through studies of first fixations (Franchini et al., 2017; Unruh et al., 2016), it's possible that first fixation findings reflected in parents of individuals with ASD in the present study may translate to social orientation differences as well, a promising avenue for future work. Taken together, parallel findings of reduced global perception across ASD parent and proband groups, and heightened local

processing in ASD probands, suggests the potential for shared underlying genetic risk for ASD that contributes to visual perceptual styles documented here.

Parent findings revealed that global visual processing differences were more subtly expressed in parents of individuals with ASD. This is consistent with our hypotheses, particularly given inconsistencies in the prior literature (Bolte & Poustka, 2006; Happe et al., 2001; Losh et al., 2009) and lack of clinical ASD symptomatology in parents—i.e., the subclinical expression of BAP traits may be more readily tapped by nuanced eye movement indices such as first fixations. In a task of language processing, for example, nuanced eye tracking differences emerged in parents, that did not surface in performance measures alone (Nayar et al., 2018). Overall, findings of generally reduced target/non-target looking in the ASD parent group, illuminate the importance of examining ASD-related traits using objective measures that can more effectively capture subtle differences reflecting genetic liability to ASD (in contrast to the lack of local/global processing in prior work in parents (Losh et al., 2010; Van Eylen et al., 2017) using performance measures alone). It may be that the eye-tracking patterns in the current study represent differential underlying mechanisms of global processing compared to controls, which may importantly relate to underlying neurobiology. Indeed, patterns of visual attention toward face stimuli in parents of individuals with ASD (Adolphs et al., 2008) have also been reflected in underlying neural correlates (Yucel et al., 2015). Future studies examining underlying neural correlates addressing timing effects of global perception (Van der Hallen et al., 2015) in both probands and parents may help to further inform findings in the present study. This work is currently underway in a separate study (Nayar, Guilfoyle, Stevens, Norton, & Losh, in prep).

Phenotypic correlates of perceptual styles

The weak central coherence or enhanced perceptual functioning theories (Bertone et al., 2005; F. Happe, 1996; Happe & Frith, 2006; Jolliffe & Baron-Cohen, 1997; Joseph et al., 2009; Kemner et al., 2008; Minshew et al., 1997; O'Riordan & Plaisted, 2001; Shah & Frith, 1983, 1993) posit that differences in perceptual styles relate to downstream ASD symptomatology (Behrmann et al., 2006; Burnette et al., 2005; Fitch et al., 2015; Happe, 1999; Jarrold et al., 2000; Jolliffe & Baron-Cohen, 2000; Klin et al., 2002b; Neufeld et al., 2020; Van der Hallen et al., 2015; Van Eylen et al., 2018). In this study, we found mixed evidence suggestive of such relationships. Robust positive relationships emerged between vacillations and exploration and incidence of RRBs in ASD, suggesting that local processing and RRBs in ASD are intricately related, and perhaps contributing to their severity. Individuals with ASD also exhibited reduced global visual processing overall, which was surprisingly related to *better* pragmatic language skills during a conversation. Similarly, parents of individuals with ASD showed parallel findings of reduced global perception relating to better pragmatic language abilities during a conversation. Conversational skills require the utilization of global strategies and the ability to also grasp details of the content from the conversational partner. Interestingly, it appears that primarily utilizing local perception during a dynamic conversation may be beneficial for families of individuals with ASD. This underscores the notion that individuals with ASD, and their family members, may be using alternative strategies to achieve the same outcome as their respective controls. Certainly, the items comprising the domains of pragmatic language in which these links were found included items such as being vague, being unable to clarify, being informal, failing to reciprocate, and failing to elaborate. Perhaps applying local strategies in a conversation that taps these global skills is compensatory for the ASD groups (e.g., being vague might be being "too" global). Though speculative, it may also be that individuals with ASD and parents of individuals with ASD may exhibit difficulty effectively switching between local and global strategies (Katagiri, Kasai, Kamio, & Murohashi, 2013) during a conversation; the positive associations with accuracy and better

pragmatic language or lack of relationships with pragmatic language in respective control groups may reflect either reduced variability, or that controls may be able to more effectively switch between local/global strategies appropriately during conversation. Given that the tasks in the present study were specifically designed to tap global processing, future studies may examine the impact of switching between local and global strategies on pragmatic language abilities among these groups. Finally, that there were no significant relationships with measures of executive functioning and local/global processing across groups in this study, highlights the specificity of low-level local/global visual processing being tapped by these tasks that may not be explained by executive functioning skills. This contributes to the ongoing debate that posits local and global processing abilities and executive functioning skills exist as standalone entities (Bolte et al., 2007; Rinehart et al., 2000; Van Eylen et al., 2017). Taken together, current findings suggest that local/global processing styles express themselves uniquely in ASD families—while on the one hand, reduced global processing relates to greater rates of RRBs, on the other hand, it is augmenting their pragmatic language skills in a conversational setting.

Finally, striking relationships between parents and their children diagnosed with ASD emerged among families affected by ASD; a finding that was not found in control parent-child pairs or in unrelated parent-child pairs across diagnostic groups. Though prior work has demonstrated shared gaze trajectories in families with typically developing individuals (Constantino et al., 2017), lack of relationships within control families in the present study is not surprising given lack of impairments in low level local/global processing in this group. Relationships of gaze in families with an affected individual are not only consistent with prior work documenting the heritability of gaze or local/global processing in ASD (Constantino et al., 2017; Neufeld et al., 2020), but also imply shared underlying biological mechanisms of local/global perception specific to families with an affected member.

Limitations and future directions

The present study should be interpreted in light of several limitations. First, while age-matched, the sample includes a wide age range. Though there is literature suggesting a developmental shift from local to global processing with age in the typical population (Nayar et al., 2015), there is unclear evidence of the perceptual maturation processes among those with ASD (although, several studies have examined perceptual abilities in younger children with ASD 7-13 (Van der Hallen et al., 2015; Van Eylen et al., 2017; Van Eylen et al., 2018) and older adults with ASD (Koldewyn et al., 2013; Mottron et al., 2003; Mottron et al., 1999). Future studies may aim to explore the developmental processes more specifically in longitudinal work. Additionally, due to the demands of the match-to-sample task in the present study, participants included high functioning individuals with ASD with intact cognitive ability. As such, findings do not generalize to the full spectrum of ASD severity. Additionally, both tasks in the present study somewhat cue global processing—the KIC paradigm specifically taps global perception as there is a requirement to integrate pacman elements to create the whole illusory shape for both target and non-target options; the Navon paradigm presents a real letter (e.g., a real S, followed by two Navon options—one large S comprised of smaller H, and one large H comprised of smaller S). As such, participants are cued to select the global match if they are primarily global processors (or they may select the local match if they are a local processor). However, it may be that presenting a real S at the beginning, primes for selection of a larger S. Future studies may wish to assess local processing preference more directly, perhaps by integrating other trials wherein a Navon hierarchical figure is first presented, followed by 2 real letters—the global match or the local match. Finally, given that BAP traits are subtly expressed in a subset of parents of individuals with ASD (Losh et al., 2011; Losh et al., 2009; Losh et al., 2008), examination of underlying neural correlates may be more fruitful than eye tracking or performance measures alone.

Indeed, recent work has documented atypicalities of local/global visual processing using KICs in individuals with ASD compared to controls (Baruth et al., 2010; Stroganova, Orekhova, et al., 2007; Stroganova et al., 2012), and more robust differences in underlying neural correlates during facial processing tasks observed among parents of individuals with ASD (Billeci et al., 2016; Yucel et al., 2015). As such, given well-studied neural circuitry of local and global visual processing (Altmann et al., 2003; T. S. Altschuler et al., 2014; Altschuler et al., 2012; Doniger et al., 2002; Doniger et al., 2000; Doniger, Foxe, et al., 2001; Fink et al., 1997; Foxe et al., 2005; Stroganova, Orekhova, et al., 2007; Stroganova et al., 2012), investigation is currently underway to better understand the neural underpinnings of visual processing styles in first-degree relatives of individuals with ASD (Nayar, Guilfoyle, et al., in prep), with goals to clarify the gene-brain-behavior relationships of visual processing and ASD.

Conclusions

This study is among the first of its kind to examine local/global perception in parents of individuals with ASD using eye tracking as a means to identify potential objective ASD-related endophenotypes and biological markers. Gottesman and Gould's (2003) classic definition of an endophenotype requires that an endophenotype 1) is specific to a disordered population and relates to its clinical-behavioral phenotypes, 2) is heritable, 3) is observable/measurable when the illness is not active, and 4) is present, albeit more subtly, among unaffected first-degree relatives with illness cosegregation. The present study's findings of robust differences in ASD and subtler reduced global processing among parents, relationships to RRBs in ASD and pragmatic language in ASD and parents, and within-family associations in families affected by ASD only, reflect 3/4 criteria. While the current study did not directly examine criteria #3, prior studies of infants who were later diagnosed with ASD demonstrate heightened visual search capabilities among 9-15 month-olds, a

pattern of gaze that predicted diagnosis of ASD at age 3 years (Cheung et al., 2018). Such findings suggest that heightened local perceptual styles are present prior to "illness" (i.e., ASD) detection, thereby implicating local/global visual perception's candidacy as an effective ASD-related endophenotype. It is additionally important to highlight the significance of the methods employed in the present study. Not only do results highlight the objective and quantifiable nature of eye tracking to capture *strategies* related to local/global processing, but they also raise important questions regarding the types of stimuli utilized in prior and ongoing work of local/global processing in ASD. The use of KICs has been extensively applied to studies of schizophrenia and typical development within the realms of vision and cognitive science, particularly given their distinct neural correlates (T. S. Altschuler et al., 2014; Altschuler et al., 2012; Foxe et al., 2001; Foxe et al., 2005; Foxe & Simpson, 2002b). Yet, studies are lacking in their application to ASD. With the addition of eye tracking, the present study was able to not only document reduced global processing in ASD, but also was able to demonstrate heightened local processing in the same study. As such, the use of KICs offers a unique stance in the examination of both levels of processing simultaneously without one interfering with the other, which is often the case in much of the work already conducted in ASD and confounds the examination of baseline perceptual strategies (Van der Hallen et al., 2015). Interestingly, underlying neural correlates of KICs documented in human subjects have also been extended to non-human primates (Feltner & Kiorpes, 2010; Sary et al., 2008), thus shedding light into its utility as a marker of underlying neurobiology that is devoid of culture, language, and higher cognitive abilities (unlike, for example, social stimuli). As such, KIC perception may be further examined in the context of an ASD-family study in cross-cultural work, which has the potential to span cultural boundaries to reveal a cross-cultural ASD-related endophenotype, and which may be used in future studies examining underlying neurobiological and molecular mechanisms of ASD.

CHAPTER 4: The neurocognitive underpinnings of global perception in ASD and first-degree relatives: A neurophysiological study of illusory contour processing

Abstract:

Background: Individuals with autism spectrum disorder (ASD) tend to show reduced or delayed global processing (i.e., the rapid, automatic integration of details for viewing and understanding the Gestalt) and an increased reliance on local perception (i.e., a focus on the details without its integration, typically a slower perceptual process). This atypical pattern of visual perception and attention has also been observed, albeit more subtly, among first degree relatives of individuals with ASD, indicating that this perceptual processing style may constitute a measurable endophenotype indexing genetic liability to ASD. Atypical neural correlates of local and global processing have also been identified in ASD, though studies have yet to investigate the underlying neurobiology of visual perception as a potential endophenotype among relatives. This study implemented electroencephalography (EEG) to extract well-established event-related potential (ERP) components resulting from perception of illusory contours in order to index the timing and response patterns of global perception in individuals with ASD and their parents.

Methods: Participants included 19 individuals with ASD (9-34 years; 53% male) and 26 parents, as well as respective control groups (n = 22 controls and n = 21 parent controls). Participants completed a passive viewing task involving Kanizsa Illusory Contours (KICs), which are often used to examine global perceptual processes, and non-illusory scrambled forms (non-KIC scramble). A visual control depicting a grid was also presented to all participants. Prior work has documented KIC perception occurring in a 2-stage process: the first perceptual phase (N1)

indexing automatic perceptual boundary completion of the illusory image, and the second conceptual phase (Ncl or N-closure) reflecting more effortful processing via a comparative process with existing neural representations. As such, both N1 and Ncl components were examined, in addition to P1, which represents early sensory registration processes. Components were examined over the parieto-occipital regions of the brain. A series of 2 X 2 repeated measures ANOVA were examined for each component separately for ASD versus controls and parent groups.

Results: Findings demonstrate expected KIC perception occurring during the perceptual phase of contour completion across groups (i.e., greater N1 negativity in response to KIC versus non-KIC scramble forms). Importantly, however N1 responses in ASD were more pronounced compared to controls across conditions, suggesting hypersensitivity to visual stimuli more broadly. Additionally, prolonged N1 latencies were observed in the ASD group relative to controls, suggesting somewhat delayed contour completion for KICs. Finally, while no significant differences were observed during the later conceptual Ncl phase, an inverted pattern of processing emerged in ASD and ASD parent groups relative to controls. Specifically, steeper Ncl amplitudes occurred in response to the non-KIC scramble versus KIC forms, while Ncl amplitudes were comparable for both conditions in control groups.

Conclusion: Findings indicate intact but relatively immature KIC perception in ASD, suggesting mild disruptions of ventral stream processes involved in global perception. Lack of differences among parents of individuals with ASD highlights the need for further investigation into the

etiology associated with clinical and subclinical features of ASD. Although non-significant, subtle but observable differences in more effortful perceptual binding components reflected in ASD and ASD parent groups suggest differences in strategies utilized to close the gap in scrambled versus KIC figures. These findings are likely indicative of heightened local perceptual processes that may run within families of ASD. Together, findings contribute to our understanding of key cognitive and neural systems affected by ASD genetic risk, with methodological strengths underscoring the efficacy of ERP/EEG methods to investigate objective markers of genetic susceptibility in ASD.

Introduction

The weak central coherence and enhanced perceptual functioning theories (Simmons & Todorova, 2018; Van der Hallen et al., 2015; Van Eylen et al., 2018; Vanmarcke, Noens, Steyaert, & Wagemans, 2017) propose that an atypical perceptual-cognitive style is evident among individuals with ASD, highlighting a dominance of local perception (a focus on the details without its integration, typically a slower perceptual process) over global perception (the rapid, automatic integration of details for viewing and understanding the Gestalt). These perceptual strategies are critical to seeing and understanding the visual world (Navon, 1977). For instance, the ability to infer the presence of a tiger behind a tree from only its head and tail has vital implications for survival. This seemingly simple ability to "fill in the gap" of missing visual information in our environment is highly complex, with specific underlying neural processes requiring both feedforward and feedback mechanisms within lower and higher-order visual areas of the brain (Doniger et al., 2002; Doniger et al., 2000; Doniger, Silipo, Rabinowicz, Snodgrass, & Javitt, 2001; Foxe et al., 2005; Foxe & Simpson, 2002b; M. M. Murray et al., 2002). A large body of literature has established links between heightened local or reduced global processing styles and symptom expression in ASD, suggesting that atypicalities in social behavior may be driven not only by regions tapping social skills (e.g., the insula), but also and less intuitively, visual or sensory areas (Keehn et al., 2020). For instance, individuals with ASD show atypicalities in global visual processing (Van der Hallen et al., 2015; Van Eylen et al., 2018), which related to social skills and verbal and nonverbal communication (Behrmann et al., 2006; Burnette et al., 2005; Happe, 1999; Jarrold et al., 2000; Jolliffe & Baron-Cohen, 2000; Klin et al., 2002a, 2002b; Van Eylen et al., 2018) as well as poorer outcomes (Fitch et al., 2015). There

is also evidence of detailed perceptual processes and atypicalities in visual attention more broadly in parents of individuals with ASD (Adolphs et al., 2008; Bolte & Poustka, 2006; Briskman et al., 2001; Chouinard et al., 2016; Constantino et al., 2017; Cribb et al., 2016; Hogan-Brown et al., 2014; M. Lee et al., 2019; Mosconi et al., 2010; Nayar et al., 2018). As such, it may be that a local and global perception and attentional differences are heritable and may be a feature that reflects genetic liability to ASD.

Many studies have examined the neural underpinnings of local and global visual perceptual processes both in typical and psychiatric (e.g., schizophrenia) (Doniger, Foxe, et al., 2001; Foxe et al., 2001; Foxe et al., 2005; Foxe & Simpson, 2002b; M. M. Murray & Herrmann, 2013) samples using Kanizsa Illusory Contours (KICs) (Kanizsa, 1976). In these KICs, the strategically placed "pac-man" elements induce an illusory shape. Typically, perceivers using a global strategy automatically experience a "pop out" effect of the illusory shape (e.g., a square) (Nieder, 2002; Ringach & Shapley, 1996), and tend to recruit brain regions associated with complex processing that are further along the visual pathway in the brain (Harris et al., 2011; Ringach & Shapley, 1996; Stanley & Rubin, 2003); however, if using a local strategy, these stimuli may be perceived as unassociated, individual "pac-man" elements, thereby relying less on neural integration and tapping into more rudimentary visual areas of the brain (T. S. Lee & Nguyen, 2001; Maertens & Pollmann, 2005).

Electroencephalography (EEG) is often used to assess neural responses to these illusions (T. S. Altschuler et al., 2014; Altschuler et al., 2012; Brown et al., 2005; Foxe et al., 2005; Kruggel et al., 2001; M. M. Murray et al., 2002; Tallon-Baudry et al., 1997), by measuring time-locked electrical activity in the brain and extracting waveforms known as event-related potentials

(ERPs). Converging evidence from studies of typical populations reveals a signature ERP response to the illusory contours (i.e., an "IC effect"), which is less robust during non-illusory figures (Ffytche & Zeki, 1996; M. M. Murray, Imber, Javitt, & Foxe, 2006; Ritzl et al., 2003). Importantly, KIC perceptual processes are considered to occur in a two-stage consolidation model, wherein the first N1 response (the IC effect) has been associated with early automatic perception of the illusory figure, without any reference to stored semantic representations of the object (Doniger et al., 2000; Foxe et al., 2005; M. M. Murray et al., 2006; M. M. Murray et al., 2002; Shpaner, Murray, & Foxe, 2009). This IC effect in adults is characterized by a larger amplitude of the early N1 component (first negative deflection) for the KIC, occurring over the lateral occipital-parietal areas of the brain (Foxe et al., 2005; C. S. Herrmann & Bosch, 2001; Proverbio & Zani, 2002; van Dinteren et al., 2014). The second, later N_{cl} response is reflective of conceptualizing the pop out image via association with appropriate stored semantic representations (i.e., identifying the illusory image as a square) (Doniger et al., 2000; Foxe et al., 2001; Foxe et al., 2005; C. S. Herrmann & Bosch, 2001; M. M. Murray et al., 2002; Proverbio & Zani, 2002; Sugawara & Morotomi, 1991; van Dinteren et al., 2014), which is linked to the lateral occipital complex across both hemispheres. The lateral occipital complex (LOC) is the visual association region considered to be the highest tier of the ventral stream or the "what" pathway involved in object recognition, and thereby is involved in integrative visual processes. The later N_{cl} response has been associated with more effortful conceptual processing when initial input may be insufficient for object recognition. The amplitude of the N_{cl} component gradually increases (becomes more negative) as stimuli becomes more complete or closeable (i.e., progressively less fragmented) (T. S. Altschuler et al., 2014; Doniger et al., 2002; Doniger et al.,

2000; Doniger, Silipo, et al., 2001; M. M. Murray et al., 2002; Sehatpour, Molholm, Javitt, & Foxe, 2006). Doniger and colleagues (2000; 2001) showed that upon boundary completion, this N_{cl} reaches a maximum amplitude (also see Doniger et al., 2002), suggesting that this N_{cl} signifies the perceptual closure of objects occurring in the ventral stream of the visual system. Together, the IC effect and N_{cl} are specific, reliable, and measurable neural markers related to illusory contour perception occurring in the lateral occipital complex of the brain.

Given this two-stage model, it was hypothesized that KIC perception may develop from more effortful to more automated processing with age (T. S. Altschuler et al., 2014), and that maturity of perception would be reflected in associated N1 and N_{cl} components, such that younger individuals would show an attenuated "IC effect" in N1 and heightened N_{cl} responses to KICs. Authors surprisingly identified similar patterns of an early stage (N1) IC effect in typically developing children as young as 6 years of age. Specifically, children and adolescents aged 6-17 years showed similar adult-like differences in N1 components while viewing illusory versus non-illusory stimuli (T. S. Altschuler et al., 2014), suggesting intact early perception of illusory images. Moreover, a prominent N_{cl} response was observed in younger children and not in adults, and the N1 latency varied inversely with age, showing that global processing may initially be immature (and more effortful) during early childhood and may follow a protracted development to discrete and automatic perceptual processing with age (T. S. Altschuler et al., 2014). Importantly, however, there appears to be evidence suggesting a U-shaped trajectory of global processing throughout development based on psychophysical and habituation studies, as prior work has shown perceptual binding or contour integration processes present in 8-month-old infants (Csibra, Davis, Spratling, & Johnson, 2000). Nonetheless, findings evidenced in neural

responses using electrophysiology importantly mirror behavioral responses (accuracy, reaction time, and eye-tracking indices) of visual processing development in neurotypical children, which demonstrates a shift from local to global processing with age (Nayar et al., 2015).

Atypical ERP response patterns to visual stimuli have been observed in individuals with intellectual disability (Shoji, Shinoda, & Ozaki, 2002), Williams Syndrome (Grice et al., 2003), and fragile X syndrome (Knoth, Vannasing, Major, Michaud, & Lippe, 2014) . In ASD, heightened local processing and reduced global processing of visual information has been observed behaviorally (Van der Hallen et al., 2015), is also evident in atypical neural responses (Isaev et al., 2020). For instance, atypical neural processing of KICs has been documented in 3-7 year old children with ASD compared to age-matched controls (Stroganova, Orekhova, et al., 2007; Stroganova et al., 2012). Specifically, though the IC effect was observed in typically developing preschoolers, an *inverted* IC effect emerged in age-matched individuals with ASD, such that the N1 amplitude (particularly in the right parietal scalp regions) was greater for the non-illusory control figure than for the KIC itself (Stroganova, Orekhova, et al., 2007). Similarly, older individuals with ASD have shown significantly prolonged N1 latencies to KICs relative to controls (Baruth et al., 2010). Baruth and colleagues concluded that sensory over-reactivity from the earlier elevated P1 amplitudes, may have caused a delay in global processing and discriminability at the N1 stage. Together, findings reflect disruptions in perceptual and attentional processes identified in underlying brain responses in ASD, which are consistent with eye-tracking findings in ASD showing reduced automatic global processing abilities for KICs (Nayar et al., 2017).

Given studies documenting sensory processing/attentional atypicalities in ASD (Chita-Tegmark, 2016; Frazier et al., 2017; Marco et al., 2011; Papagiannopoulou et al., 2014; Robertson & Baron-Cohen, 2017), hypothesized to result from cortical hyperexcitability in ASD (Takarae & Sweeney, 2017), sensory components become important to examine within the context of KIC perception. Indeed, neural correlates of responses to KICs extend beyond the N1 and N_{cl} ERPs, but have been insufficiently explored in ASD. For instance, P1 and P2, P3 components have also been implicated in KIC perception and are believed to index early sensory processing in extrastriate visual areas (Foxe et al., 2001; Foxe et al., 2005), visual categorization (M. J. Herrmann, Ehlis, Ellgring, & Fallgatter, 2005), and attentional processes more generally (C. S. Herrmann & Mecklinger, 2001; C. S. Herrmann et al., 1999; C. S. Herrmann et al., 2004; van Dinteren et al., 2014). P1 is atypical in schizophrenia, showing significantly diminished amplitudes relative to controls (Foxe et al., 2001; Foxe et al., 2005; Knebel, Javitt, & Murray, 2011; Wynn et al., 2015). In a few studies, P2 and P3 have shown protracted developmental trajectories (Baruth et al., 2010; van Dinteren et al., 2014). While studies have shown prolonged latencies and atypical amplitudes in these components towards general visual stimuli and KICs in ASD (Baruth et al., 2010; Milne, Scope, Pascalis, Buckley, & Makeig, 2009; Sokhadze et al., 2009; Stroganova, Orekhova, et al., 2007), such sensory components remain to be deeply investigated in this population.

Together, atypical perception of KICs has been observed at both the behavioral and neural levels in young typically developing children and children with ASD. However, it remains unknown whether the neural underpinnings of local and global perceptual processes index genetic liability to ASD and may be measurable in unaffected relatives more subtly, constituting

ASD-related endophenotypes (Gottesman & Gould, 2003). Indeed, many cognitive features of ASD are heritable and evident among relatives in more subtle forms (Losh et al., 2011; Losh et al., 2009; Losh et al., 2008; Losh et al., 2012; Losh & Piven, 2007; Piven, Palmer, Jacobi, et al., 1997; Piven, Palmer, Landa, et al., 1997). Specifically, first-degree relatives of individuals with ASD may exhibit milder characteristics that are associated with ASD but are not associated with functional impairment (i.e., the broad autism phenotype; BAP). These traits are thought to disaggregate within an individual (i.e., social aloof features or rigid tendencies versus having both) and tend to have fewer clinical comorbidities (and therefore reduced polygenic influence), helping to address the biological basis related to ASD. The study of biological relatives can help unlock clues as to how genes may play a role in ASD-related features across the heterogeneous spectrum, with the expression of susceptibility genes ranging from clinical impairment to more subtle personality, language, and cognitive styles. An endophenotype approach may aid research efforts to identify more homogenous, meaningful subgroups of affected individuals so as to identify potential biomarkers related to ASD, further elucidating gene-brain-behavior relationships related to ASD phenotypes. Clarifying such phenotypic patterns may eventually allow for stratification of families in biologically and clinically meaningful ways and allow for more targeted and effective diagnostics and interventions.

EEG methodology more broadly may be particularly fruitful in identifying biomarkers related to the BAP that may reflect genetic liability to ASD. For instance, studies investigating neural electrical activity have found differences in activity levels among siblings of individuals with ASD (Levin, Varcin, O'Leary, Tager-Flusberg, & Nelson, 2017; Orekhova et al., 2014; Tierney et al., 2012), as well as among parents who exhibit features of the BAP (Billeci et al.,

2016; Dawson et al., 2005; Mehdizadehfar, Ghassemi, Fallah, & Pouretemad, 2020). Specifically, Dawson et al. (2005) identified atypical latencies and amplitudes of N170 ERP responses to faces among parents of individuals with ASD compared to control participants, which were related to lower performances on behavioral tasks involving face recognition and object memory. Using functional MRI and face stimuli blurred to highlight certain features of the face, Adolphs and colleagues (2008) showed that parents with the BAP demonstrated striking behavioral and neurological similarities to individuals with ASD (Dalton et al., 2005; Frazier et al., 2017; Kleinhans et al., 2008; Klin et al., 2002a; Pelphrey et al., 2002) during facial processing, such that they devoted less attention to the eye region of the face compared to controls, and in tandem exhibited increased activity in the amygdala and fusiform gyrus (Yucel et al., 2015). These studies therefore highlight the importance of using objective and sensitive neural measures to capture subtle biological differences in the BAP, which may reflect genetic liability to ASD.

The aim of the present study is to explore the neurophysiological signature of visual perception in individuals with ASD and parents, compared to respective control populations. Underlying neural differences were assessed using electroencephalography (EEG) during a paradigm of visual processing (KIC, scrambled KIC, and a visual control). Early ERP (event-related potential) components of the ventral stream (i.e., N1 and P1) were examined across stimuli, in addition to the later onset N_{cl} component. Prior work has documented that the P1 arises from generators in both dorsal ("where") and ventral ("what") pathways in the parieto-occipital areas (Heinze et al., 1994; Mangun, Hopfinger, Kussmaul, Fletcher, & Heinze, 1997; M. M. Murray, Foxe, Higgins, Javitt, & Schroeder, 2001; M. M. Murray, Foxe, Higgins,

Schroeder, & Javitt, 2001; Simpson, Foxe, Vaughan, Mehta, & Schroeder, 1995), and reflects early sensory processing or registration of stimuli. As such, and consistent with prior work documenting heightened P1 responses in ASD (Baruth et al., 2010), we predicted that individuals with ASD would show elevated P1 amplitudes compared to typically developing controls, while parents of individuals with ASD will show comparable P1 responses to parent controls. The N1 occurs following the P1 and confers the initial stages of form or feature discrimination in the lateral occipital complex of the ventral stream (Allison, Puce, Spencer, & McCarthy, 1999; Mouchetant-Rostaing, Giard, Bentin, Aguera, & Pernier, 2000; Ungerleider, 1982; Vogel & Luck, 2000). Atypical N1 responses may therefore reflect ventral stream disruptions of early perceptual processes. Given prior evidence of attenuated N1 amplitudes in certain electrodes (Stroganova, Orekhova, et al., 2007), and evidence documenting perceptual binding atypicalities in ASD, it is predicted that individuals with ASD will demonstrate reduced N1 mean amplitude and prolonged N1 latencies reflecting immature ventral stream processes indicative of automatic global processing impairments. Given that parents of individuals are not clinically impaired and that atypical sensory processing has not been evidenced in this group, no differences in N1 amplitudes are predicted to occur between parent groups, as this measure reflects early visual perception of the stimuli. Finally, while the P1 is considered to tap general sensory processing or registration of visual information, and the N1 taps the *perceptual* phase of boundary closure, the N_{cl} is thought to reflect the *conceptual* phase of processing that is more effortful and occurs during a later time window than the perceptual phase. The N_{cl} is typically larger in magnitude (more negative) for easily closeable images like the KIC in this task and attenuated or less negative for images that are more fragmented (such as the non-KIC scramble condition in this

task). Disruptions in the N_{cl} component may signify dysfunction in the LOC (Doniger et al., 2002; Doniger et al., 2000; Doniger, Silipo, et al., 2001), particularly given its occurrence during a later time window. As such, it is hypothesized that attenuated N1 mean amplitudes in ASD will impact downstream N_{cl} amplitudes, indicating less automatic perceptual binding and conceptualization of the illusory image. It is similarly hypothesized that parents of individuals with ASD will demonstrate atypicalities in this level of KIC perception as well, perhaps also showing attenuated N_{cl} amplitudes in response to KICs compared to parent controls. Both attenuated amplitudes towards KICs in ASD and ASD parents may therefore represent disruptions in the LOC.

Additionally, this study sought to explore whether neural responses to KICs aggregate within families of individuals with ASD, with the predictions that significant positive correlations will emerge between parent-child pairs within ASD families. Finally, this study examines how underlying neural correlates may relate to clinical and subclinical traits associated with the ASD phenotype, including social communication, patterns of sensory processing, and repetitive/rigid behaviors among both individuals with ASD and parents. Given that local and global visual processing have been shown to relate to downstream social communication in individuals with ASD (Behrmann et al., 2006; Burnette et al., 2005; Fitch et al., 2015; Happe, 1999; Jarrold et al., 2000; Jolliffe & Baron-Cohen, 2000; Klin et al., 2002b; Van Eylen et al., 2018), it is hypothesized that N1 and N_{cl} components may relate to pragmatic (social) language and repetitive or rigid behaviors in ASD and parents, while P1 components may show associations with sensory processing. Findings from this study may help to unpack the potential biological origins of local and global processing in individuals with increased liability to ASD.

Methods

Participants.

Eighty-eight participants were included in this study, including 19 individuals with ASD (ASD group), 22 controls (control group), 26 parents of individuals with ASD (ASD-parent group) and 21 parent controls (parent-control group). Parent-child dyads in this study included 15 ASD and 19 control dyads (i.e., 4 individuals with ASD and 3 control participants did not have a parent with valid data participate in the study). Participants were recruited from ongoing studies, with additional outreach efforts made via word of mouth and recruitment through local clinics and registries. Inclusion criteria for all participants were as follows: 1) English as their first language, 2) a minimum full-scale IQ (FSIQ) of 70, 3) no uncorrected visual impairment(s) (e.g., strabismus, uncorrected double vision), 4) no history of neurological conditions (e.g., brain injury, seizures), and 5) no known genetic syndrome associated with ASD or major psychiatric disorder (i.e., bipolar, schizophrenia, and related psychotic disorders). Parents of individuals with ASD were defined by having a child diagnosed with idiopathic ASD. Control participants were required to have no personal or family history of ASD or related genetic conditions (e.g., fragile X syndrome), as well as no nuclear family member with a history of depression or language-related delays. See ***Table 1*** for characteristics of the sample. All study procedures were approved by Northwestern University's Institutional Review Board and written informed consent/assent was obtained for all participants.

Clinical-behavioral Characterization.

Assessment of Cognitive Level. The Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) or the Wechsler Intelligence Scale for Children—Third Edition (WISC-III) was used to assess either a 2-subtest IQ or a full-scale (FSIQ), verbal, and performance IQ. The ASD group had a significantly lower IQ (full-scale, verbal, and performance IQs) than the control group (*p*s < .01). Group differences in IQ did not emerge between parents. There were no age differences between proband or parent groups.

Assessment of ASD Symptoms. The Autism Diagnostic Observation Schedule-General or 2nd Edition (ADOS) (Lord et al., 2000; Lord et al., 2012) and/or the Autism Diagnostic Interview-Revised (ADI-R) (Lord et al., 2012; Lord, Rutter, & Le Couteur, 1994) were administered at the research or intra-lab reliable scoring and administration level, to confirm a diagnosis of ASD. ADOS calibrated severity scores were additionally calculated (Hus & Lord, 2014), and following prior work (Cuccaro, Shao, Grubber, Slifer, Wolpert, Donnelly, Abramson, Ravan, Wright, DeLong, et al., 2003; Richler, Bishop, Kleinke, & Lord, 2007b), the repetitive sensorimotor behavior (RSMB) factor scores were computed from the ADI-R.

Table 4.1: *Sample Characteristics*

	Control Group			ASD Group			Group Difference		
	M	**Range**	**SD**	**M**	**Range**	**SD**	***t***	**df**	***p***
Probands n (M/F)		**22 (12/10)**			**19 (10/9)**		-	-	-
Age (years)	13.95	7.66-22.03	3.75	15.83	9.10-34.23	6.13	-1.20	39	0.238
FSIQ	120.98	88-145	13.35	97.26	70-130	15.40	5.28	39	**0.000**
VIQ	122.60	98-142	11.42	96.11	69-136	18.29	5.55	38	**0.000**
PIQ	117.29	79-149	18.75	97.45	68-125	17.59	3.44	38	**0.001**
ADOS Total Severity Score^	-	-	-	8.24	5-10	1.52	-	-	-
SA Severity Score	-	-	-	7.88	4-10	1.58	-	-	-
RRB Severity Score	-	-	-	8.59	6-10	1.06	-	-	-
Parents n (M/F)		**21 (3/18)**			**26 (4/22)**		-	-	-
Age (years)	46.75	33.77-59.04	7.41	48.67	35.68-59.70	7.12	-0.90	45	0.371
FSIQ	118.52	94-135	11.27	115.5	88-135	12.82	0.86	45	0.395
VIQ	116.55	97-130	10.84	112.6	86-130	13.70	1.04	42	0.305
PIQ	113.85	92-127	9.77	113.5	89-130	11.50	0.10	42	0.925

Bold indicates significance $p < .05$; Italics indicates unequal variance assumed; ^Comparison severity score labels are as follows: 0-2 = “minimal-to-no evidence”, 3-4 = “low”, 5-7 = “moderate”, 8-10 = “high”. ADOS, Autism Diagnostic Observation Scale; FSIQ, Full-Scale IQ; PIQ, Performance IQ; RRB, Restricted and Repetitive Behaviors and Interests; VIQ, Verbal IQ.

Assessment of the Broad Autism Phenotype in Parent-ASD Group. BAP traits (i.e., sociability, rigidity, and pragmatic language) were assessed among parents of individuals with ASD using a semi-structured interview (the Modified Personality Assessment Scale-Revised (MPAS-R), (Tyrer, 1988) that has been extensively utilized in prior work (Piven, Palmer, Landa, et al., 1997). BAP features were coded following methods outlined in prior work (Losh et al., 2009; Losh et al., 2008; Piven, Palmer, Landa, et al., 1997) (Losh et al., 2009; Losh et al., 2008; Piven, Palmer, Landa, et al., 1997)—raters were blind to family diagnosis and assigned scores from 0 to 2 (trait absent, possibly present, definitely present) on a 5-point (0.5 increment) Likert scale. Finally, the broad autism phenotype questionnaire (BAP-Q) (Hurley et al., 2007) was additionally utilized to characterize BAP traits continuously via self-report.

Assessment of Sensory Processing.

In addition to the ADI-R RSMB factor score (Cuccaro, Shao, Grubber, Slifer, Wolpert, Donnelly, Abramson, Ravan, Wright, DeLong, et al., 2003; Richler et al., 2007b), the Short Sensory Profile 2[133] or Adult/Adolescent Sensory Profile (Brown, Tollefson, Dunn, Cromwell, & Filion, 2001; Dunn, 1994) were additionally obtained from a subset of individuals to further characterize ASD-related sensory symptomatology in both individuals with ASD and parents of individuals with ASD.

Design and Stimuli.

General Procedures. Participants completed a passive-viewing task displaying trials of illusory (KIC squares; *Fig. 4.1a*) and non-illusory (KIC scramble; *Fig. 4.1b*) images, as well as a visual

control stimulus (Grid; *Fig. 4.1c*). Unique to this study, the grid was utilized for sensitivity analyses to determine whether potential differences observed in illusory and non-illusory conditions may be explained by general visual perceptual processes alone versus perceptual closure-related processes specifically. Participants sat in a large comfortable cushioned chair, held a button box in their hands throughout the experiment, and had a stool placed beneath their feet for additional comfort and support. All participants sat at a distance of 60cm from the center of a computer screen, in a dimly lit room. Finally, there was a research scientist present in the room approximately 1 meter behind the participant for the entirety of the experiment to assist with behavioral management strategies if needed.

Task and Stimulus (*Fig. 3.1)*. Consistent with prior work (Stroganova, Orekhova, et al., 2007; Stroganova et al., 2012), all 3 test stimuli subtended a total width and height of 9.44 x 9.44 cm (i.e., 9 x 9°) at a 60cm viewing distance. The illusory square and pac-man radius subtended 5.66 x 5.66 cm (i.e., 5.4 x 5.4°) and 1.89 cm (i.e., 1.8°), respectively. Luminance was set at 0 (black) and 1 (white) for all test stimuli, with "pac-man" elements set to black, and brightness of the computer screen lowered to ~70% to remove after-image effects. Screen size was 55.5 x 32 cm.

The paradigm was programmed on Presentation® Software (Version 21.1, www.neurobs.com). Each test stimulus (i.e., KIC square, KIC scramble, and Grid) were presented in random order for a total of 150 times per participant, with a maximum of 4 successive repetitions of the same stimulus, for a total of 450 test trials. Test stimuli were presented for 500 ms per trial, with an inter-stimulus interval (ISI) set between 1700 and 2000 ms to prevent any potential after-image effects.

To increase engagement and alertness and to maintain adequate attention (Luck, 2004), a combination of behavioral and experimental procedures were implemented. Experimental procedures included: 1) 35 embedded grey-scale "visual break trials" to prevent visual fatigue from test stimuli, which were displayed for 850 ms and occurred after 8-25 test trials; 2) 20 embedded "attention trials" displaying an image of a set of colorful balloons of unlimited duration and requiring a button press to advance the experiment; 3) 21 embedded colorful "progress trials" of 2000 ms depicting an animate character climbing up a mountain reflecting the participant's progress through the experiment. The progress trials were set to display after 15-25 test trials. As such, the ratio of experimental attention and progress trials to test trials was set to 1:6. Finally, at the half-way point of the full paradigm, participants had the option to take a break for an unlimited duration.

In addition to a research scientist's presence in the room, behavioral management strategies included: 1) a social story outlining the details related to the EEG visit that was sent to participants prior to their appointment, and then was reviewed again during their in-person visit; 2) task instructions with engaging images and an embedded interactive practice to sit still and use the button box appropriately; 3) a mnemonic outlining the rules for successful EEG data (i.e., A=stay Awake, B=press the Button when you see the Balloons, C=Calm and still your body, face, and hands, D=Don't speak while looking at the pictures, E=keep your Eyes on the screen); 4) a comfortable environment (i.e., quiet room, white and empty walls, black skirt placed over the table to cover environmental visual noise sure as cables and EEG equipment, comfortable chair, stool for feet); 5) a sensory or comforting toy that the participant brought with them if needed; 6) and finally, implementation of mini breaks in addition to the pre-programmed half-

way point break if the participant appeared to be falling asleep, becoming fidgety, or displaying other behaviors reflective of reduced engagement and alertness. The testing room was equipped with a camera placed atop the monitor, capturing the participants' face. As such, the examiner responsible for running the experiment was able to see the participant at all times, thereby ensuring that the experiment was paused during blank screens (i.e., not on test or stimuli trials) to check in with the participant as needed.

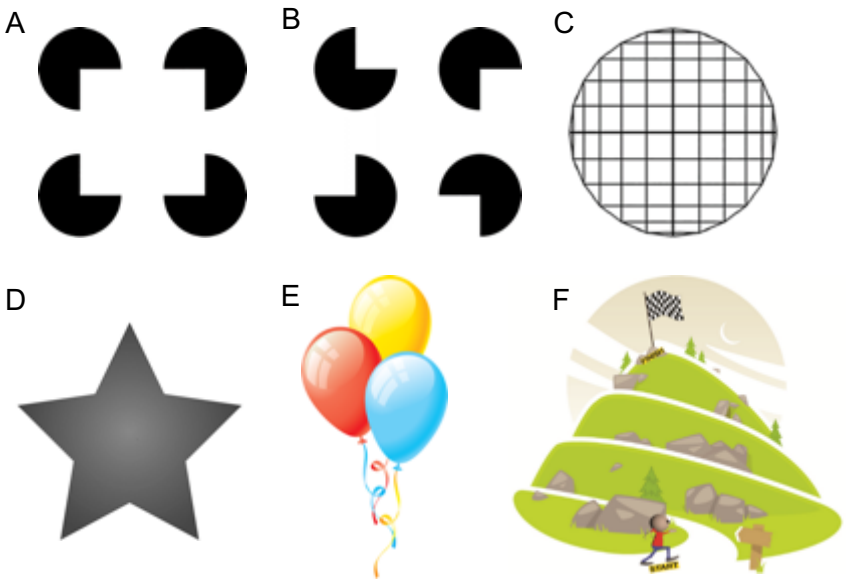

Figure 4.1. *Passive viewing stimuli presented in a pseudo-random order. A) KIC (150 trials), B) non-KIC scramble (150 trials), C) grid control (150 trials), D) visual break (35 trials), E) attention (20 trials), and F) progress (21 trials).*

EEG Data Acquisition. EEG was recorded using the Biosemi ActiveTwo System (Biosemi B.V., Amsterdam). Recordings were made in a single-ended mode that amplifies the differences between a common mode sensor (CMS) electrode and each other electrode site, with referencing occurring off-line. Given the presence of a driven right leg (DRL), and pre-amplifiers at each

electrode site, as well as high electrical isolation, impedance did not need to be reduced via abrasion (Kappenman & Luck, 2010). Offset was kept below 40 μV for each electrode for all but one individual; this participant's electrodes were examined showing > 40 μV on two electrodes of interest (PO3 and PO4). These electrodes were interpolated, and data were re-examined showing identical statistical results with or without this participant included. As such, to increase power and maximize sample size, this individual was included in all subsequent analyses.

Each participant's head circumference was measured. Active Ag-AgCl electrodes were affixed to an elastic cap that was appropriate for the participant's head size (Electro-Cap Inc., Eaton, OH). EEG was recorded from 32 sites arranged in 10-20 system positioning (electrodes at locations Fp 1/2; AF 3/4; F 7/3/z/4/8, FC 5/1/2/6, C 3/z/4, T 7/8, CP 5/1/2/6, P 7/3/z/4/8, PO 3/4, and O 1/z/2). Right and left mastoids were also recorded via external electrodes, with all participants' data re-referenced offline to these electrodes. Finally, electro-oculogram was recorded from the lateral canthus of the right eye and infraorbital ridge of the left eye. EEG was recorded with a low-pass hardware filter with a half-power cutoff at 104 Hz and digitized at 1,024 Hz with 24 bits of resolution.

EEG Data Processing. All processing utilized EEGLAB version 2019.0 (Delorme & Makeig, 2004) and ERPLAB version 7.0.0 (Lopez-Calderon & Luck, 2014) Toolboxes in MATLAB version R2019a Update 6 (MATLAB, 2010). Data were re-sampled at 512 Hz (Stroganova, Orekhova, et al., 2007), and high-pass filtered at 0.1 Hz. All trials were first baseline-corrected to the prestimulus interval, then epoched (100 ms pre- to 600 ms post-stimulus) to each of the test trials of interest (i.e., KIC square, KIC scramble, Grid). All trials during which a button press occurred were removed to avoid including the effect of motor

movements; this occurred rarely during test trials. Individual channels depicting excessive noise or were specifically influenced by the 60 Hz electrical noise (i.e., only one channel showing a spike at 60 Hz) were interpolated (with no more than 3 channels per participant, and no more than 1 electrode of interest per participant). On average, a total of n=15 (n=4 parent control, n=4 ASD parent, n=4 control proband, n=3 ASD proband) participants' data had channel(s) interpolated, with an average of n=1 channel per participant (1 channel was interpolated for 14 participants, and 2 channels were interpolated for 1 participant). There were no group differences between ASD and controls ($t(5) = -1.2$, $p = .29$), and parent groups ($t(6) = 1.0$, $p = 1.0$), in the number of channels needing interpolation.

Artifact detection to remove epochs during which blinks or horizontal eye movements occurred, as well as to remove movement and muscle artifacts, was performed using a multi-step process. For eye electrodes, a new bipolar eye channel was generated for vEOG using Fp1 and Fp2, which are located on the forehead and thus are sensitive to blinks [i.e., biVEOG = (Fp1 + Fp2)/2] (Luck, 2014b; Luck, Lopez-Calderon, Huang, Arita, & Foo, 2017; Trujillo, Stanfield, & Vela, 2017). All trials with blinks and large eye movements were rejected based on the criteria of having a bivEOG amplitude that was consistent with a blink (typically 75 μV), that occurred during the duration of the test trial presentation (i.e., 0-500ms from stimulus onset). For scalp channels, artifact detection was performed using moving window peak-to-peak for epoched data, with the threshold set for any epoch that exceeded a minimum of +/- 100 μV at any electrode site (except for T7/T8 channels), to remove noise due to muscle tension or movement. Finally, artifact detection was implemented with a more liberal threshold (i.e., +/- 115 μV) for T7 and T8 channels due to muscle noise or cardiac artifact. Each epoch was subsequently visually inspected

for accuracy of artifact detection. Horizontal eye movements in the hEOG channel that were not concurrently flagged with blinks were additionally manually removed.

Final number of trials included in analyses are presented in ***Table 2***. There were no differences in the number of trials remaining following artifact rejection between ASD and control groups or between parent groups. After artifact rejection, epochs of each trial type were averaged. Finally, data were re-referenced to an average scalp reference. For plotting purposes, a low-pass filter was applied at 30 Hz.

Table 4.2: *Number of trials remaining following artifact detection and rejection*

	Control Group				**ASD Group**				**Group Difference**		
	M	SE	Min	Max	M	SE	Min	Max	t	df	*p*-value
Total	280.27	12.64	156	360	267.37	19.04	123	418	0.58	39	.566
KIC	93.73	4.45	50	126	88.26	6.71	37	141	0.70	39	.491
Non-KIC	92.45	4.37	49	127	87.11	6.67	44	140	0.69	39	.495
Grid	94.09	4.29	53	122	92.00	6.09	40	137	0.29	39	.776

	Parent Control Group				**ASD Parent Group**				**Group Difference**		
	M	SE	Min	Max	M	SE	Min	Max	t	df	*p*-value
Total	296.33	14.43	134	407	297.96	9.77	206	384	-0.10	45	.924
KIC	99.62	5.03	43	137	100.19	3.49	63	134	-0.10	45	.924
Non-KIC	94.95	4.94	44	137	97.69	3.08	69	127	-0.49	45	.627
Grid	101.76	4.72	47	133	100.08	3.71	67	130	0.29	45	.777

Components examined and electrodes of interest (EOI)

Area measures in time windows of interest, including mean amplitude and fractional area latency (15% area onset latency) (Luck, 2004, 2014b) were examined as outlined below. Area measures (versus peak measures) were selected as they are less sensitive to noise and differences in number of trials (Clayson, Baldwin, & Larson, 2013; Luck, 2014c; Luck & Kappenman, 2018). See ***Figures 4.2 and 4.3*** for scalp maps.

EOIs were examined for consistency across scalp sites to determine whether averaging across hemispheres and regions (i.e., occipital and parieto-occipital regions) was possible. Scalp plots were examined separately for probands and parents. EOIs demonstrated polarity consistencies (i.e., negative or positive) across hemispheres in each group. Given lack of evidence of lateralization across P1 and N1 components in particular (e.g., Baruth et al., 2010; Foxe et al., 2005), left, right, and center electrodes were averaged for occipital electrodes along with the left and right parieto-occipital electrodes. Specifically, an average parieto-occipital EOI was generated from five electrodes, including O1/Oz/O2/ and PO3/PO4 (T. S. Altschuler et al., 2014; Baruth et al., 2010). This approach was designed to increase power to detect differences and to reduce unnecessary noise that may occur from heterogeneity present in ASD and across individual electrodes. Additionally, prior work has shown that PO3 and PO4 sites elicit the largest IC effects (T. S. Altschuler et al., 2014; Foxe et al., 2005), with object processing and boundary completion occurring bilaterally in the human brain (see seminal papers Doniger et al., 2000; Doniger, Foxe, et al., 2001). Conducting group X condition analyses at the averaged EOI level is therefore a more parsimonious and statistically rigorous method than examining each electrode separately by hemisphere.

P1 mean amplitude ($P1_{amp}$) was examined as a measure of early sensory processing. Given more positive P100 mean amplitudes emerging in ASD compared to controls for the KIC (Baruth et al., 2010), P1 mean amplitude was a specific component of interest in this study to 1) replicate prior work, and 2) to examine potential differences among parents. P1 mean amplitude were examined over the comprehensive parieto-occipital EOI.

N1 mean amplitude ($N1_{amp}$) was additionally included as a component of interest given a wealth of research documenting significant N1 responses to KICs in the typical population (T. S. Altschuler et al., 2014; Altschuler et al., 2012; Foxe & Simpson, 2002b; M. M. Murray & Herrmann, 2013; M. M. Murray et al., 2006; M. M. Murray et al., 2002), with some attenuation observed among boys with ASD (Stroganova, Orekhova, et al., 2007). Similar to the P1 component, the N1 mean amplitude component will also be examined across the comprehensive parieto-occipital EOI.

N1 onset mean latency ($N1_{lat}$) or, N1 fractional area latency (15% area latency), was similarly examined across the comprehensive parieto-occipital EOI, particularly due to documented prolonged latency differences emerging over all parieto-occipital regions in response to KICs in ASD compared to controls (Baruth et al., 2010). Neurotypical literature has used a combination of peak and onset latencies (T. S. Altschuler et al., 2014; Altschuler et al., 2012; Foxe & Simpson, 2002; M. M. Murray et al., 2002).

N1 closure mean amplitude ($N1_{cl}$) was the final component examined, and is typically identified between ~230ms and 400ms over the lateral occipital regions of the brain (T. S. Altschuler et al., 2014; Doniger et al., 2000; Doniger, Silipo, et al., 2001; Foxe et al., 2005; M. M. Murray et al., 2006; Shpaner, Molholm, Forde, & Foxe, 2013).

Selection of Time Windows and Outlier Detection

Component windows were determined by examining the grand average across KIC and scramble conditions and electrode sites of interest (comprehensive parieto-occipital EOI—i.e., O1/z/2, PO3/4), separately for probands and parents. Separate windows were established for probands and parents given that most ERP components develop with age (see *Table 3*). Component windows for the grid control condition were also established separately, given observed latency differences following examination of group averaged waveforms.

Using established component windows, data were then examined for outliers as follows. Probands and parents were separately examined with diagnostic groups collapsed, for outliers 3SD above or below the mean for each individual electrode site of interest, ERP component, (i.e., mean amplitude and fractional area latency for N1 and mean amplitude for P1) and condition (i.e., KIC, scramble, grid). Two participants (1 parent control and 1 ASD proband) were consistent outliers on most electrodes and conditions and components and were therefore excluded from subsequent analyses.

Following exclusion of these two participants, a new grand average was generated, component windows were assessed and confirmed for consistency with prior thresholds, and data were re-assessed for additional outliers based on the final comprehensive parieto-occipital EOI of interest. Subsequent analyses excluded participants if their parieto-occipital EOI measurement was 3SD above or below the mean for each component and condition separately. Final sample across conditions included 19 individuals with ASD and 22 controls across all four components. For parents, final sample size included 21 parent controls across all but one component (N_{cl} mean amplitude; n = 20). There were 25 ASD parents for the N1 mean amplitude component,

with a full sample contributing data (i.e., n = 26) for the P1 and N_{cl} mean amplitudes and N1 mean onset latency components.

Statistical Analysis

Assumptions testing.

Data were examined to ensure model assumptions of statistical tests (i.e., repeated measures ANOVAs) were met. The EOI per component and per condition were examined separately for proband groups and parent groups, with most assumptions being met adequately as follows: 1) the dependent variable is being measured at the continuous level; 2) independent variables consist of two categorical, related groups; 3) outliers have been removed upon analyses (see "Data Quality Examination" above); 4) residual errors were all normally distributed based on examination of Q-Q plots, and outcome variables were mostly normally distributed based on histograms and Shapiro-Wilk's test (with the exception of the N1 and P1 amplitudes across KIC and non-KIC scramble conditions for proband groups only when combining diagnostic groups). Importantly, N1 and P1 amplitudes were normally distributed within diagnostic groups. Finally, the 5th assumption, which assumes that the variances of the differences between all combination of related groups must be equal, is not able to be assessed in a 2X2 (condition X group) repeated measures ANOVA. In this design, because there are only 2 levels of repeated measures, there is only one set of difference scores with no additional comparisons being made to indicate a violation of sphericity. As such, all assumptions for the 2X2 repeated measures ANOVA were met.

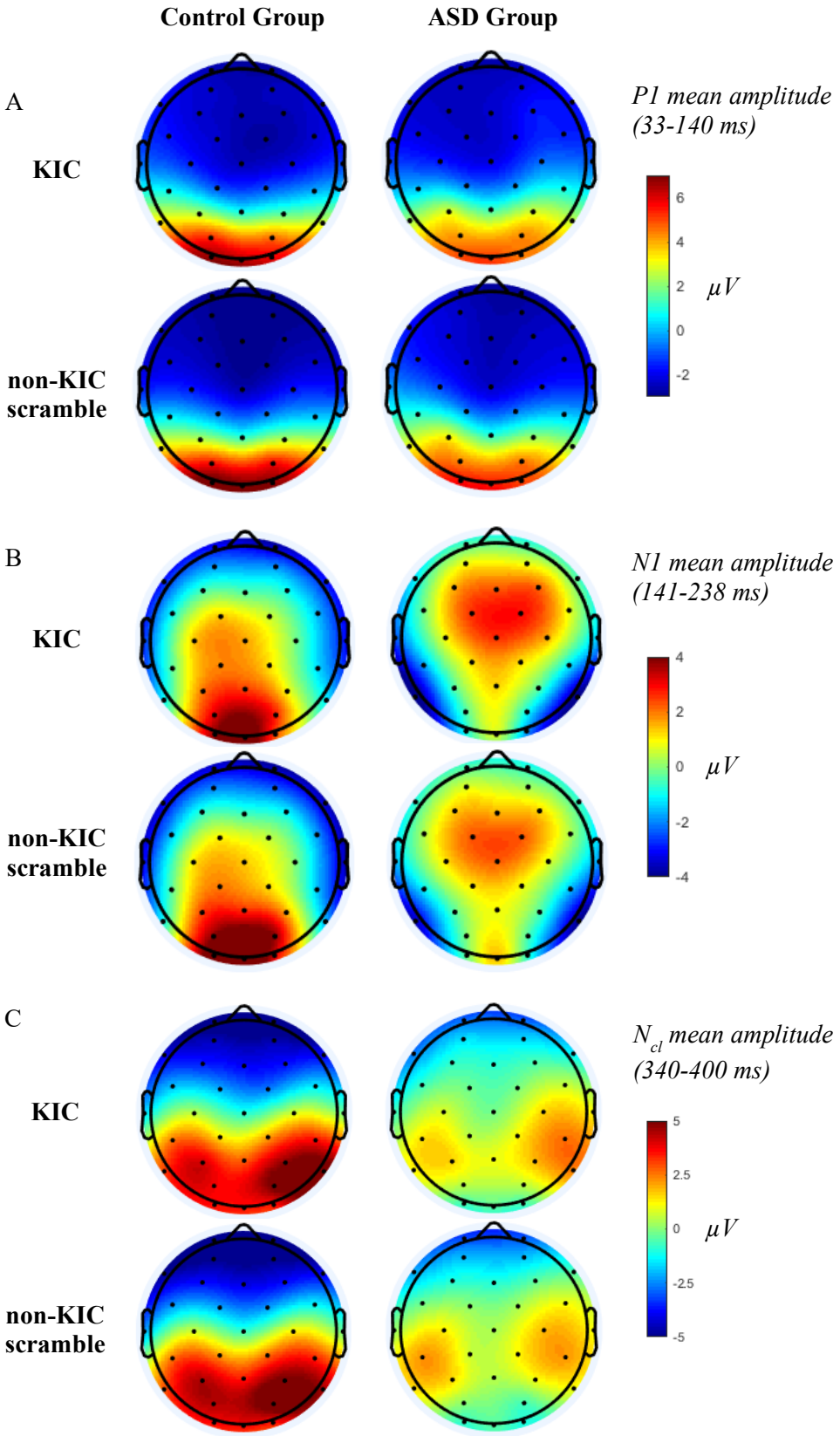

Figure 4.2. *Scalp maps depicting A) P1 mean amplitude (33-140 ms), B) N1 mean amplitude (141-238 ms), and C) N_{cl} mean amplitude (340-400 ms) in individuals with ASD (right) compared to the control group (left) across KIC (top) and non-KIC scramble (bottom) conditions.*

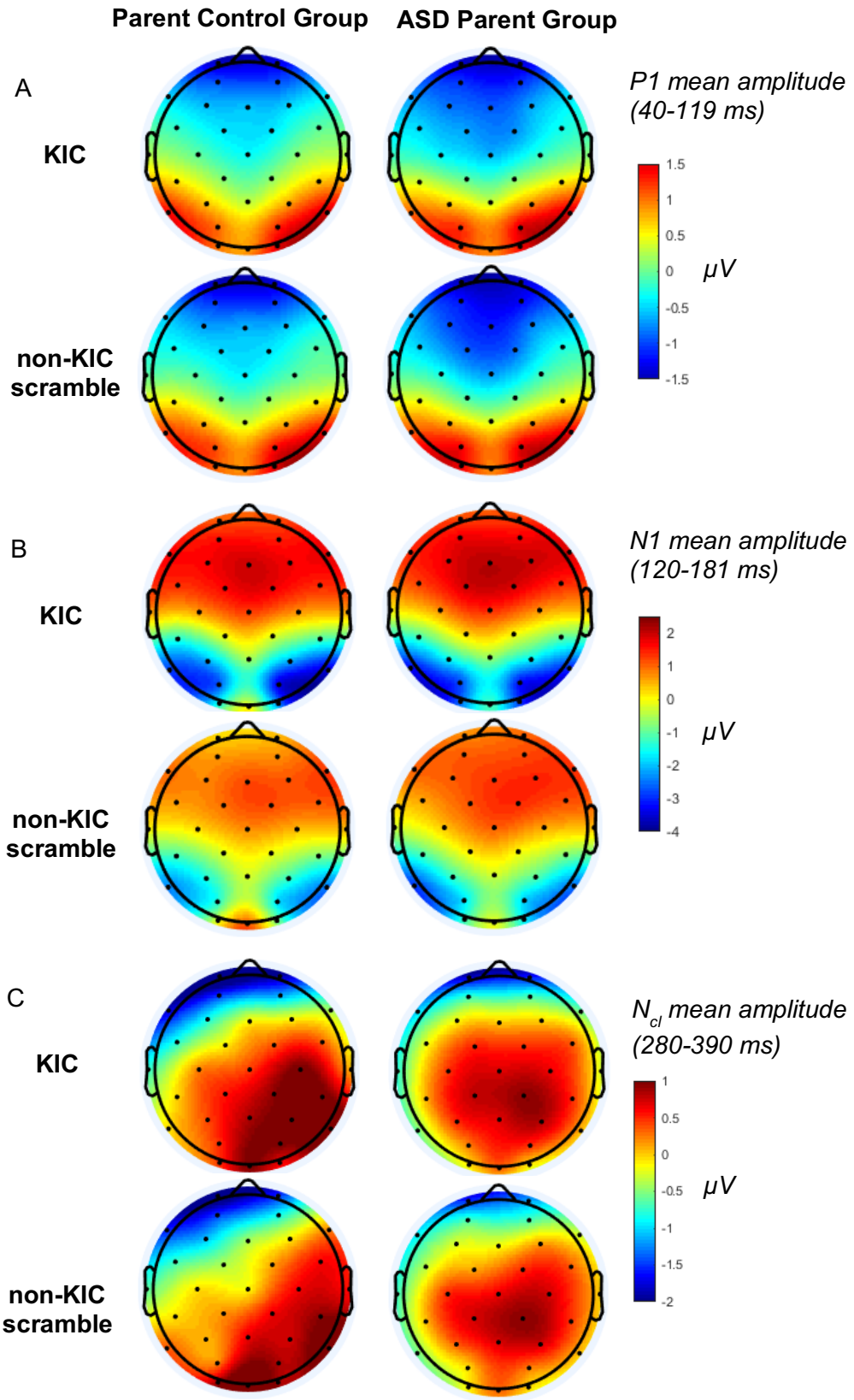

Figure 4.3. *Scalp maps depicting A) P1 mean amplitude (40-119 ms), B) N1 mean amplitude (120-181 ms), and C) N_{cl} mean amplitude (280-390 ms) in parents of individuals with ASD (right) compared to the parent control group (left) across KIC (top) and non-KIC scramble (bottom) conditions.*

Table 4.3: *ERP component time windows of measurement*

	P1	N1	Ncl
KIC and non-KIC scramble conditions			
Probands	33-140	141-238	340-400
Parents	40-119	120-181	280-390
Grid control condition only			
Probands	47-166	167-207	-
Parents	51-92	93-148	-

Covariates

Given the wide age range across proband groups, despite groups being well-matched on other factors (see Table 1), proband ERP data were examined in relation to age to explore potential age effects. Not surprisingly, and consistent with the developmental literature (T. S. Altschuler et al., 2014; Brandwein et al., 2011; Gomes et al., 2001), overall, there were significant correlations between age and P1 amplitude across groups and within ASD and control groups separately (rs < -.50, ps < .05). Following a median split in age (<13 years and >13 years), though sample sizes were smaller, diagnostic group differences in ERP components for individuals in the younger age bracket were different than the findings emerging between groups for individuals in the older age bracket, suggesting key developmental influences on ERP components in response to illusory contour perception across groups. As such, age was included as a covariate in all analyses involving proband groups.

1. Group Differences.

Because the IC effect is based on the difference between KIC and non-KIC conditions, a 2 (ASD versus control) by 2 (KIC versus non-KIC scramble condition) repeated ANOVAs

(rmANOVAs) was employed. This type of analysis (similar to calculating difference waves) allowed the removal of any common source waveforms (Luck, 2014a) from generators responding merely to general visual information, and help to isolate and reveal the time course of components. All rmANOVA significance levels were two-tailed and set to $p < .05$ and were adjusted using the Benjamini-Hochberg method (Benjamini & Hochberg, 1995) using a false discovery rate (FDR) of .10. FDR level of .10 (as opposed to .05) was selected to adjust for multiple tests without potentially missing important effects (APA, 1994a). All univariate ANOVA analyses (i.e., control grid condition reported below) were also adjusted using the same Benjamini-Hochberg correction method at the .10 FDR level. Both raw *p*-values and p_{adj}-value are reported in tables 4-5, and were only conducted on primary analyses.

KIC versus non-KIC scramble conditions.

Analyses only included KIC and non-KIC scramble conditions. A series of 2X2 rmANOVAs were conducted for each component with one between-group factor (diagnostic group—i.e., ASD versus control) and one within-group factor (condition—i.e., KIC versus non-KIC scramble). Age was taken as a covariate for proband groups. Post-hoc pairwise comparisons were only conducted if the effects of condition, group, or group X condition interaction term were significant.

Control grid condition.

To assess whether KIC and non-KIC scramble ERP findings were due to perceptual differences more broadly, group differences were first examined separately for proband (ASD versus control

groups) and parent (ASD parent and parent control groups) groups on the control grid condition. A series of univariate ANOVAs were conducted for *a priori* selected components (i.e., P1 mean amplitude and N1 mean amplitude given that these early sensory and perceptual components are expected to be observed across visual stimuli, while N1 latency and Ncl components were reserved primarily to examine IC effects) between diagnostic groups. Age was included as a control variable for proband groups.

Secondary analyses

Absolute ratio of the difference waves between N1 and P1.

Given that the trajectories of the ERPs differed greatly between the ASD and the control groups, it is possible that the IC effect and mean amplitudes of the N1 and N_{cl} components varied substantially in relation to the amplitudes of the earlier components (i.e., P1). As such, supplementary analyses were conducted in both parent and proband groups as follows. Consistent with the typical development literature (T. S. Altschuler et al., 2014), additional ANOVAs were conducted on the absolute values of the ratio between the KIC vs. non-KIC scramble conditions during the N1 and P1 amplitudes. This allowed us to assess the significance of the relative differences in trajectories emerging from the initial P1 amplitude. In other words, the smaller the ratio of the difference between KIC and non-scramble conditions between N1 and P1, the less modulation in the early perceptual phase of KIC perception, and the larger the ratios, the more modulation occurred (T. S. Altschuler et al., 2014). The absolute ratio between P1 and N1 was also applied to the control grid condition, particularly given differences in trajectories in

proband groups, with differences examined between diagnostic groups for proband and parent groups separately.

Age differences in ASD versus control groups.

As mentioned earlier, given the wide age range and documented differences in the development of ERPs examined here (T. S. Altschuler et al., 2014), a 2 X 2 rmANCOVA was re-applied to the ASD and control groups only, with a median split in age (median = 13.89 years) resulting in a younger sample and an older sample. The younger sample included 7 individuals with ASD and 13 controls, with 12 and 9, respectively, included in the older sample. Age was still included as a covariate in this model due to documented differences across the ages comprised within each younger/older sample (T. S. Altschuler et al., 2014). Given reduced power from smaller sample sizes, trends in results are reported alongside to aid in the interpretation of potential differences emerging between younger and older individuals.

2. Parent-Child Associations.

To examine familiality of underlying neural correlates of local/global processing, each component for each condition was used to examine parent-child associations. Specifically, linear regression models were employed separately for each family diagnosis (i.e., ASD families and control families), between parent and child pairs. All analyses included within-family relation nested within the model as a random effect to control for spousal relationships with the same child. Child age was added as a control variable for all analyses.

3. Associations with Eye Tracking.

Pearson (for mean amplitude components) and Spearman (for fractional area latency component, due to its reduced range) correlations were examined between components in each condition and eye-tracking indices derived from an interactive match-to-sample task of local/global processing using KICs (Nayar, Winston, et al., in prep) separately for parents and probands (diagnostic groups combined). The eye tracking variable included in associations with underlying neural correlates of global perception obtained in this study includes a Global-Local Composite z-score that includes both performance (i.e., accuracy and reaction time) measures and a suit of eye-tracking variables. The composite z-score characterizes global versus local looking patterns, with higher z-scores indicating more global processing, and lower z-scores reflecting greater local processing.

4. Associations with Clinical-Behavioral Correlates.

Spearman correlations between components in each condition and ASD or broad autism phenotype (BAP) clinical-behavioral features were examined in the ASD and ASD parent groups. For individuals with ASD, ADOS total and subscale (social affect and restricted and repetitive behaviors) calibrated severity scores and ADI-R scores were examined. Given the sensory nature of the components being assessed in the present study, the AASP and SSP2 were additionally included in correlation analyses. For parents of individuals with ASD, BAPQ total and sub-scores (i.e., pragmatic, aloof, and rigid), MPAS aloof, rigid, and untactful scores, as well as AASP scores for sensory processing were examined.

Results

Refer to ***Figures 4.4 - 4.6*** for waveform and component window depiction by group.

1. Group Differences.

Control grid condition (Table 4.4). *Probands.* N1 amplitude was significantly larger in the ASD group compared to the control group ($F_{(1,38)} = 17.68$, $p < .0001$, partial $\eta^2 = .318$). No significant group differences emerged in P1 mean amplitude ($F_{(1,38)} = .75$, $p = .391$, partial $\eta^2 = .019$). Examination of absolute ratios of the N1 amplitude and the P1 amplitude revealed no significant group differences ($F_{(1,38)} = .027$, $p = .871$, partial $\eta^2 = .001$). *Parents*. No significant group differences emerged across any component examined ($P1_{amp}$ $F_{(1,45)} = 2.56$, $p = .117$, partial $\eta^2 = .054$; $N1_{amp}$ $F_{(1,45)} = .59$, $p = .446$, partial $\eta^2 = .013$). Similarly, the absolute ratio between N1 and P1 mean amplitudes revealed no significant differences ($F_{(1,45)} = 1.41$, $p = .242$, partial $\eta^2 = .030$).

KIC versus non-KIC scramble conditions (Tables 4.5 - 4.6)

Early Sensory Processing (P1 component).

P1 mean amplitude. Probands. Repeated measures ANOVA revealed no significant group effects between the ASD and control groups ($F_{(1,38)} = .29$, $p = .594$, partial $\eta^2 = .008$). Additionally, no condition ($F_{(1,38)} = 1.84$, $p = .183$, partial $\eta^2 = .046$) or group X condition ($F_{(1,38)} = .37$, $p = .545$, partial $\eta^2 = .010$) effects emerged. *Parents.* Parent findings showed no differences in group ($F_{(1,45)} = .45$, $p = .504$, partial $\eta^2 = .010$), condition ($F_{(1,45)} = .42$, $p = .520$, partial $\eta^2 = .009$), or group X condition interaction ($F_{(1,45)} = 1.59$, $p = .214$, partial $\eta^2 = .034$).

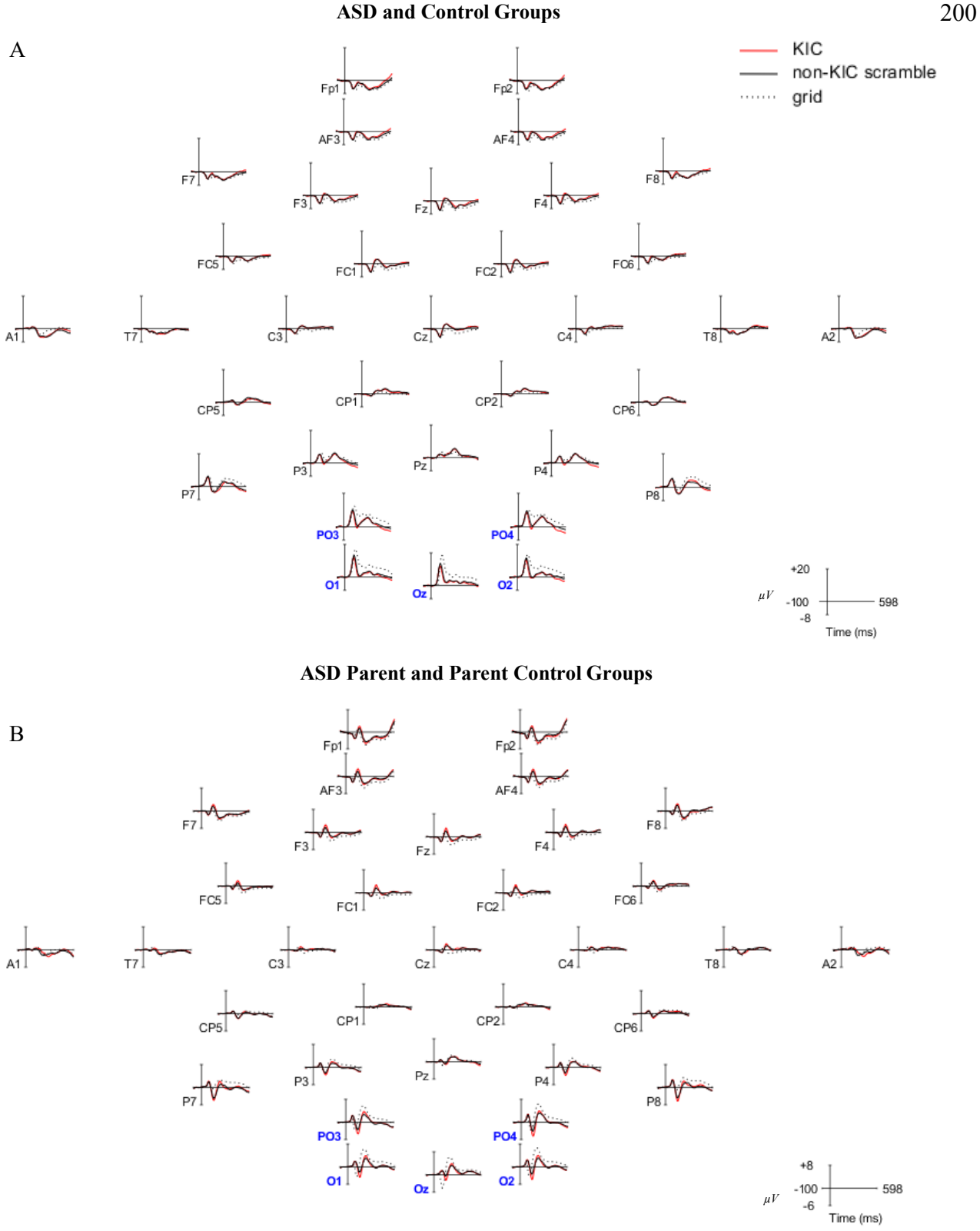

Figure 4.4. *Grand average waveforms for KIC, non-KIC scramble, and grid control conditions in A) individuals with ASD and controls, and B) parents of individuals with ASD and parent controls. Blue bolded electrodes represent the comprehensive EOI utilized in analyses.*

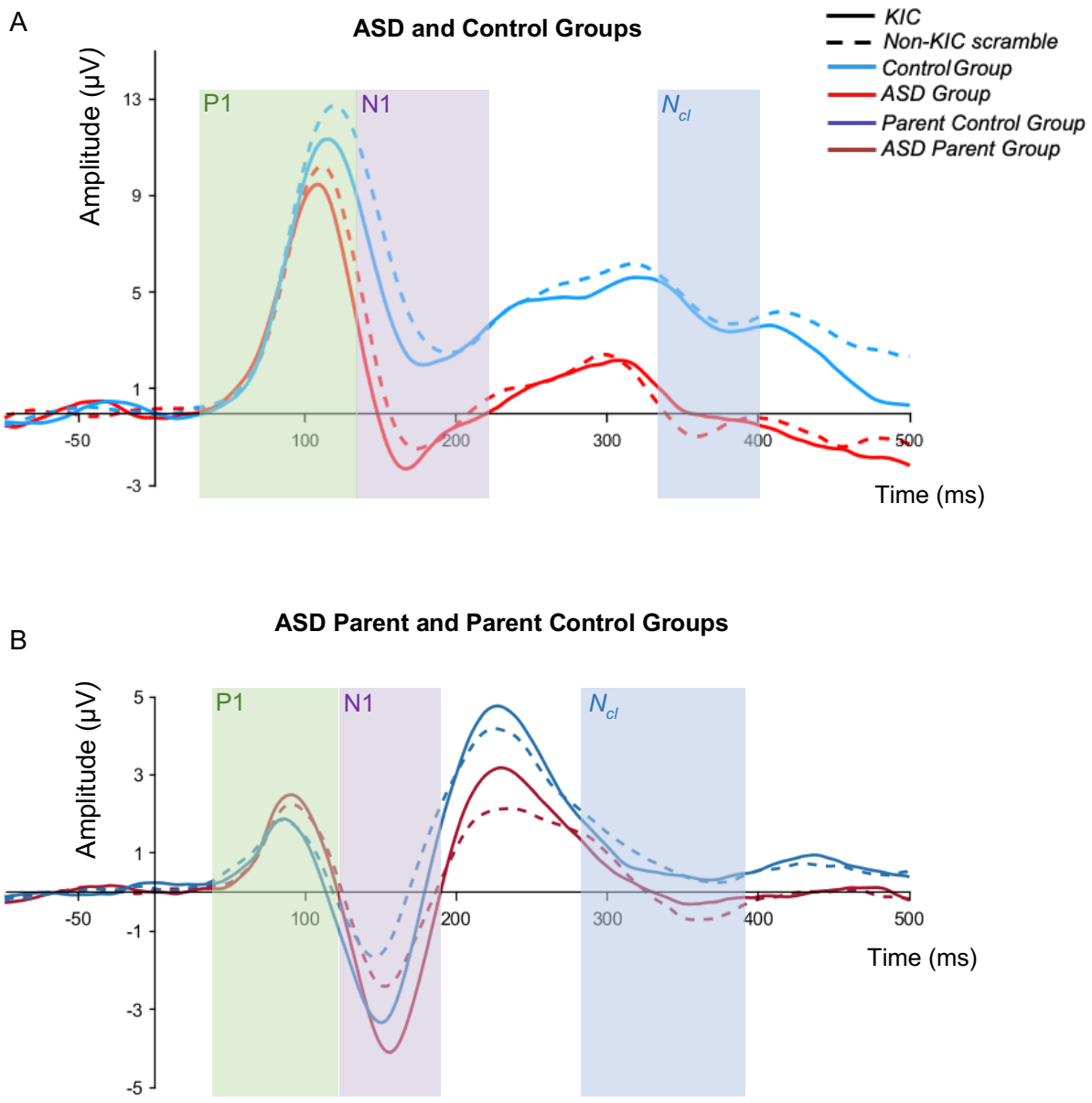

Figure 4.5. *Group average waveforms for KIC (solid) and non-KIC scramble (dashed) conditions in A) individuals with ASD (red) and controls (blue), and B) parents of individuals with ASD (dark red) and parent controls (dark blue).*

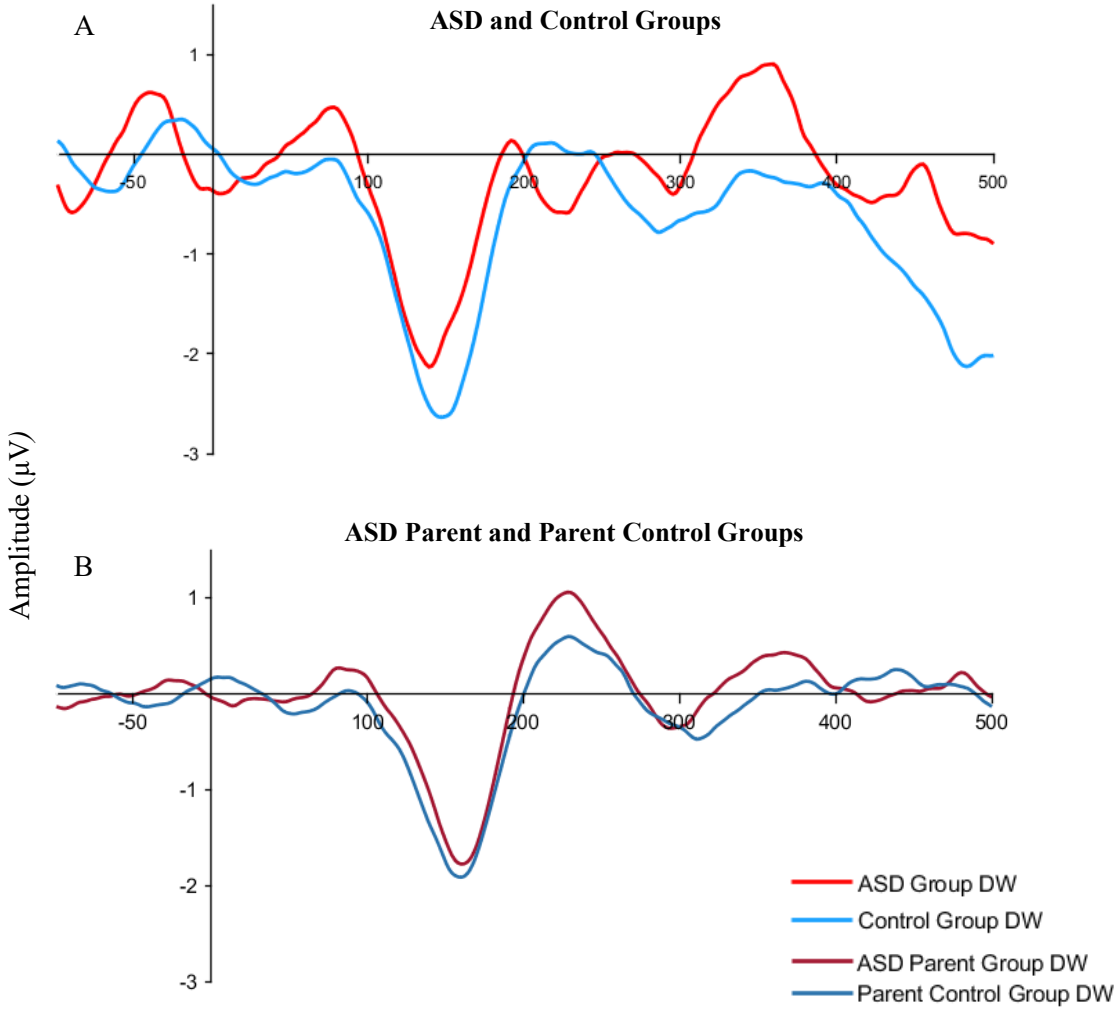

Figure 4.6. *Group average difference waves between KIC minus non-KIC scramble conditions in A) individuals with ASD (red) and controls (blue), and B) parents of individuals with ASD (dark red) and parent controls (dark blue).*

Table 4.4: *Summary of Results - Grid control*

	M (SD)	**M (SD)**	***F***	***df***	**partial η²**	***p***	***padj^***
	Control Group	**ASD Group**					
P1 amplitude	8.85 (6.41)	6.48 (3.86)	0.75	1,38	0.02	0.391	0.587
N1 amplitude	10.43 (6.18)	3.21 (3.98)	17.68	1,38	0.32	**0.000**	**0.000**
N1:P1 IC difference	1.78 (1.38)	6.27 (23.94)	0.03	1,38	0.00	0.871	0.871
	Parent Control Group	**ASD Parent Group**					
P1 amplitude	0.25 (1.53)	1.01 (1.71)	2.56	1,45	0.05	0.117	0.351
N1 amplitude	-2.64 (3.53)	-1.74 (4.27)	0.59	1,45	0.01	0.446	0.446
N1:P1 IC difference	7.99 (10.92)	21.65 (51.73)	1.41	1,45	0.03	0.242	0.363

Bold indicates $p < .05$; ^padj included Benjamini-Hochberg correction at a false discovery rate of .10.

Illusory Contour Processing (N1 component)

N1 mean amplitude. *Probands*. A significant effect of group ($F_{(1,38)} = 6.68$, $p < .05$, partial $\eta^2 = .15$) demonstrated that the ASD group had greater amplitude N1 negativity than the control group. Additionally, a significant condition effect (i.e., the IC effect) ($F_{(1,38)} = 7.42$, $p = .01$, partial $\eta^2 = .163$) showed that the N1 mean amplitude was more negative during the KIC than during the non-KIC scramble condition. *Parents.* N1 mean amplitudes did not significantly differ between ASD parent and parent control groups, indicating no main effect of group ($F_{(1,44)} = .04$, $p = .841$, partial $\eta^2 = .001$). There was, however, the expected perceptual IC effect ($F_{(1,44)} = 37.96$, $p < .0001$, partial $\eta^2 = .549$), where N1 negativity was enhanced during the KIC versus the non-KIC scramble condition for both groups. There was no group X condition interaction effect ($F_{(1,44)} = .52$, $p = .475$, partial $\eta^2 = .012$).

N1 onset latency. *Probands*. Although there was no main effect of group ($F_{(1,38)} = .06$, $p = .808$, partial $\eta^2 = .002$), there was a significant main effect of condition ($F_{(1,38)} = 5.96$, $p < .05$, partial $\eta^2 = .136$), with a trending group X condition interaction ($F_{(1,38)} = 3.42$, $p = .072$, partial $\eta^2 = .083$), such that the N1 onset latency was prolonged in the KIC condition for the ASD group compared to the control group. *Parents.* Similar to proband groups, while there was no group ($F_{(1,45)} = .05$, $p = .819$, partial $\eta^2 = .001$) or group X condition interaction ($F_{(1,45)} = .19$, $p = .666$, partial $\eta^2 = .004$), there was a main effect of condition ($F_{(1,45)} = 7.89$, $p < .01$, partial $\eta^2 = .149$) such that the onset of the N1 was prolonged for the KIC versus the non-KIC scramble condition across groups.

Ncl mean amplitude. *Probands*. There was a significant main effect of group ($F_{(1,38)} = 5.64$, $p < .05$, partial $\eta^2 = .129$) indicating more negativity in the ASD compared to the control group. There were no condition ($F_{(1,38)} = .00$, $p = .99$, partial $\eta^2 < .0001$) or condition X group interaction effects ($F_{(1,38)} = 1.12$, $p = .296$, partial $\eta^2 = .029$). *Parents*. There were no significant main effects of group ($F_{(1,45)} = .39$, $p = .550$, partial $\eta^2 = .008$), condition ($F_{(1,45)} = .13$, $p = .719$, partial $\eta^2 = .003$), or their interaction ($F_{(1,45)} = .77$, $p = .384$, partial $\eta^2 = .017$) in parent groups.

Table 4.5: *Summary of Results – descriptives and repeated measures ANOVA for KIC and non-KIC conditions*

	KIC	**non-KIC scramble**	**KIC**	**non-KIC scramble**
	M (SD)	**M (SD)**	**M (SD)**	**M (SD)**
	Control Group		**ASD Group**	
P1 amplitude	5.82 (4.32)	6.55 (4.82)	4.63 (2.97)	5.04 (3.08)
N1 amplitude	3.29 (5.56)	4.22 (5.39)	-0.78 (4.36)	-0.08 (3.42)
N1 latency	154.21 (7.22)	153.98 (9.45)	157.23 (10.57)	153.86 (10.94)
Ncl amplitude	3.89 (5.12)	4.15 (6.20)	-0.14 (4.67)	-0.59 (5.09)
	Parent Control Group		**ASD Parent Group**	
P1 amplitude	0.94 (1.21)	1.09 (1.22)	1.3 (1.53)	1.25 (1.33)
N1 amplitude	-2.13 (2.88)	-0.71 (2.48)	-2.17 (3.36)	-1.01 (2.89)
N1 latency	132.11 (6.72)	130.11 (7.51)	132.04 (7.02)	129.67 (6.54)
Ncl amplitude	0.33 (2.10)	0.55 (2.06)	0.16 (1.90)	0.07 (1.70)

Component/ Measure	***F***	***df***	**partial η^2**	***p***	***padj***
	ASD versus Control groups Main Effect of Group				
P1 amplitude	0.29	1,38	0.01	0.594	0.792
N1 amplitude	6.68	1,38	0.15	**0.014**	**0.069**
N1 latency	0.06	1,38	0.00	0.808	0.970
Ncl amplitude	5.64	1,38	0.13	**0.023**	**0.069**
	Main Effect of Condition				
P1 amplitude	1.84	1,39	0.05	0.183	0.365
N1 amplitude	7.42	1,38	0.16	**0.010**	**0.069**
N1 latency	5.96	1,38	0.14	**0.019**	**0.069**
Ncl amplitude	0.00	1,38	0.00	0.989	0.989

Group X Condition Interaction					
P1 amplitude	0.37	1,39	0.01	0.545	0.792
N1 amplitude	0.01	1,38	0.00	0.940	0.989
N1 latency	0.34	1,38	0.08	*0.072*	0.173
Ncl amplitude	1.12	1,38	0.03	0.296	0.507
ASD parent versus Control parent groups					
Main Effect of Group					
P1 amplitude	0.45	1,45	0.01	0.504	0.825
N1 amplitude	0.04	1,44	0.00	0.841	0.841
N1 latency	0.05	1,45	0.00	0.819	0.841
Ncl amplitude	0.36	1,44	0.01	0.550	0.825
Main Effect of Condition					
P1 amplitude	0.42	1,45	0.01	0.520	0.825
N1 amplitude	53.50	1,44	0.55	**0.000**	**0.000**
N1 latency	7.89	1,45	0.15	**0.007**	**0.042**
Ncl amplitude	0.13	1,44	0.00	0.719	0.841
Group X Condition Interaction					
P1 amplitude	1.59	1,45	0.03	0.214	0.825
N1 amplitude	0.52	1,44	0.01	0.475	0.825
N1 latency	0.19	1,45	0.00	0.666	0.841
Ncl amplitude	0.77	1,44	0.02	0.384	0.825

Bold indicates $p < .05$; ^padj included Benjamini-Hochberg correction at a false discovery rate of .10.

Secondary analyses

Absolute ratio of the difference waves between N1 and P1.

<u>*Probands*</u>. There were no significant differences between individuals with ASD versus control participants in the absolute ratio of the difference waves (KIC minus non-KIC scramble condition) of N1 to P1 mean amplitudes ($F_{(1,38)} = .67$, $p = .417$, partial $\eta^2 = .017$). <u>*Parents*</u>. Similarly, the N1:P1 difference wave ratios were comparable between parent groups ($F_{(1,44)} = .34$, $p = .656$, partial $\eta^2 = .008$).

Table 4.6: *Summary of Secondary Analyses N1:P1 IC difference*

	M (SD)	**M (SD)**	***F***	***df***	**partial η^2**	***p***
	Control Group	**ASD Group**				
N1:P1 IC difference	4.16 (7.60)	3.05 (3.71)	0.67	1,38	0.02	0.417
	Parent Control Group	**ASD Parent Group**				
N1:P1 IC difference	9.85 (15.77)	7.60 (10.42)	0.34	1,44	0.01	0.565

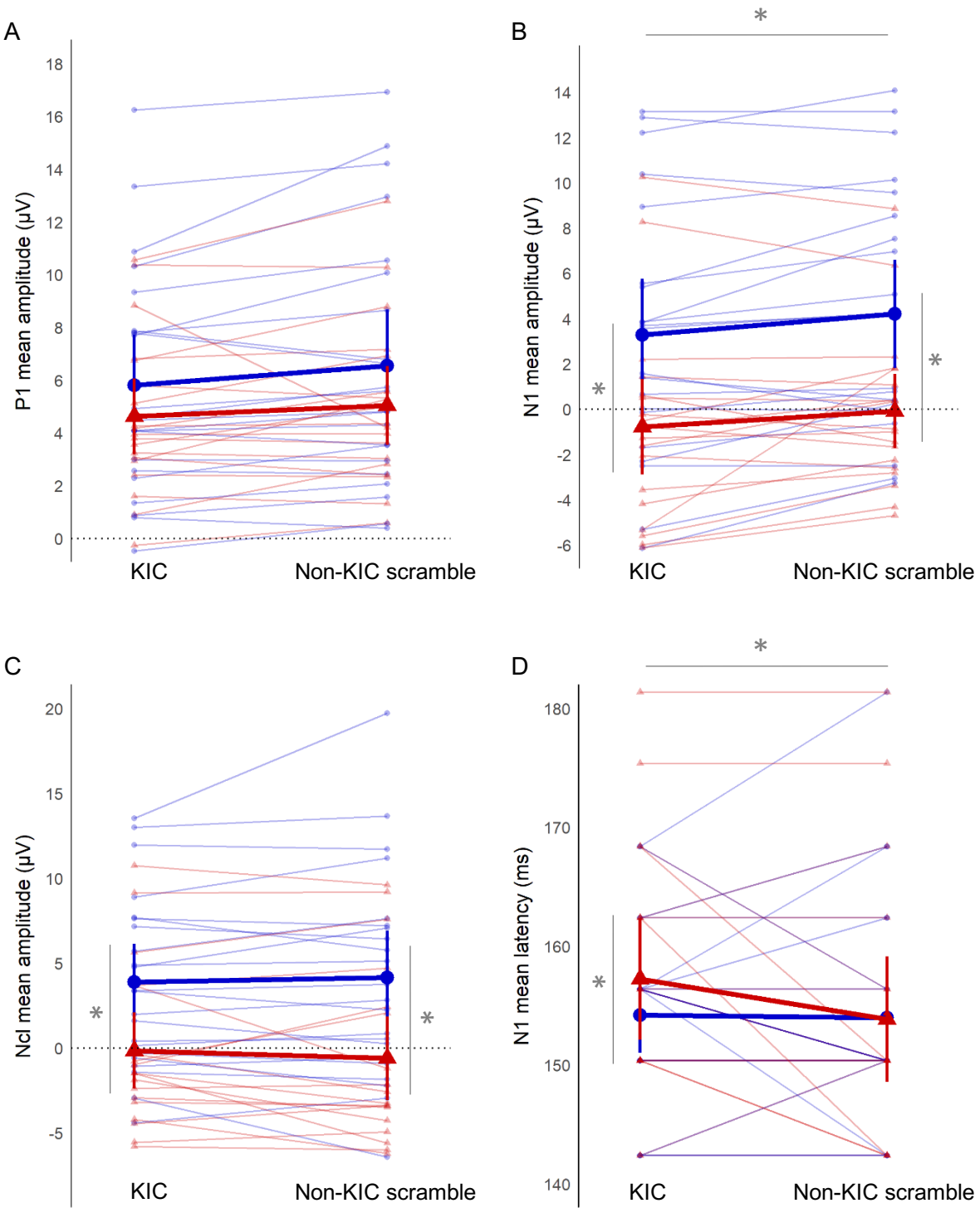

Figure 4.7*. Diagnostic group differences between the ASD group (red) and the control group (blue) across KIC (left) and non-KIC scramble (right) conditions for A) P1 mean amplitude, B) N1 mean amplitude, C) N_{cl} mean amplitude, and D) N1 fractional area onset latency (15%), which depicts overlapping data for multiple participants.*

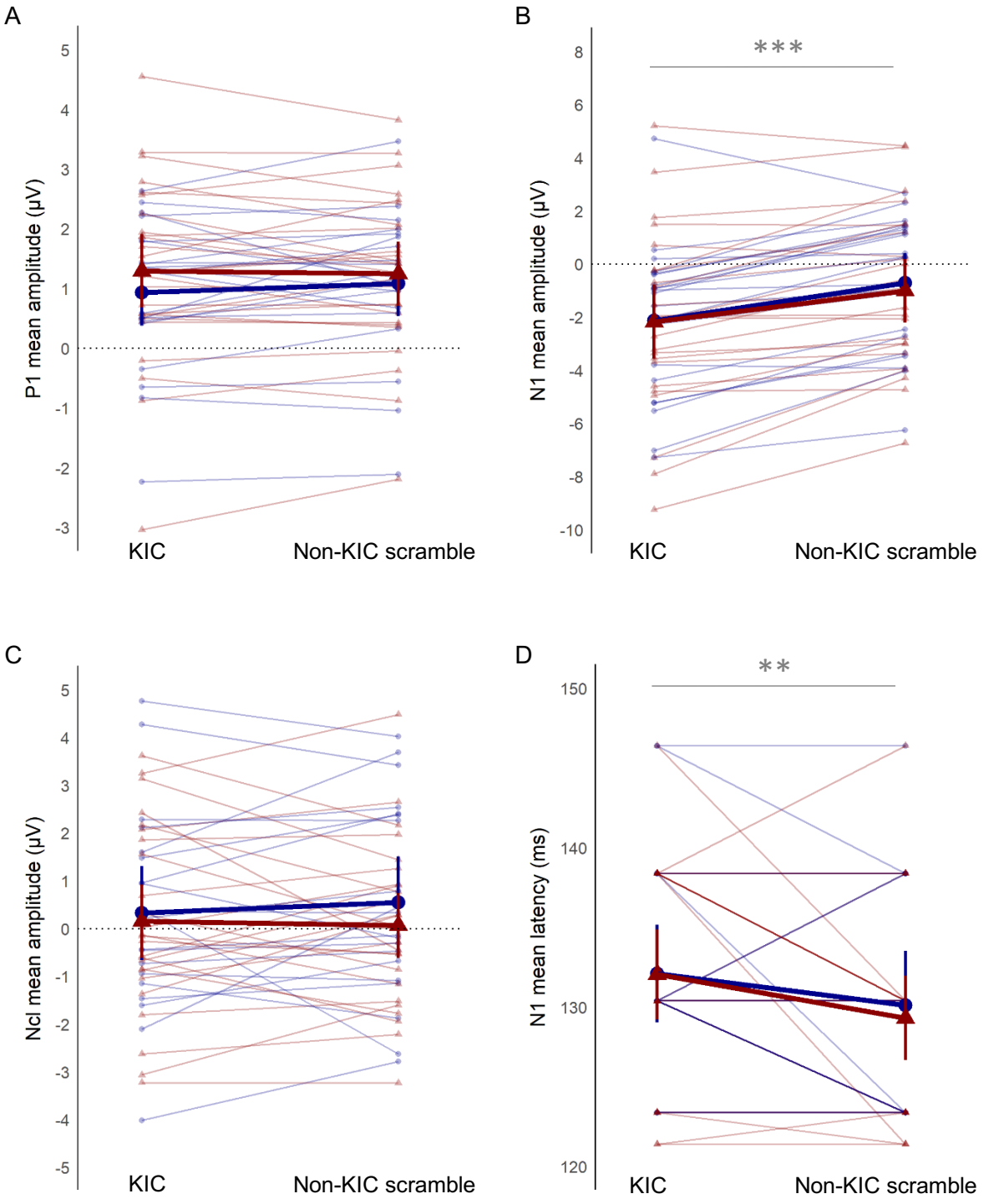

Figure 4.8. *Diagnostic group differences between the ASD parent group (dark red) and the parent control group (dark blue) across KIC (left) and non-KIC scramble (right) conditions for A) P1 mean amplitude, B) N1 mean amplitude, C) N_{cl} mean amplitude, and D) N1 fractional area onset latency (15%), which depicts overlapping data for multiple participants.*

Parent Control Group
ASD Parent Group
$^{**}p < .01$; $^{***}p < .001$

Age differences in ASD versus control groups.

P1 mean amplitude. No significant group differences emerged between younger or older participants with ASD versus controls (*younger* $F_{(1,17)} = .32$, $p = .581$, partial $\eta^2 = .018$; *older* $F_{(1,18)} = .04$, $p = .839$, partial $\eta^2 = .002$). No condition (*younger* $F_{(1,17)} = .13$, $p = .719$, partial $\eta^2 = .008$; *older* $F_{(1,18)} = .08$, $p = .782$, partial $\eta^2 = .004$) or group X condition (*younger* $F_{(1,17)} = .61$, $p = .444$, partial $\eta^2 = ..035$; *older* $F_{(1,18)} = .66$, $p = .427$, partial $\eta^2 = .035$) effects emerged for either age group.

N1 mean amplitude. Though there were trending group differences among the younger groups (*younger* $F_{(1,17)} = 4.01$, $p = .061$, partial $\eta^2 = .191$; *older* $F_{(1,18)} = 2.27$, $p = .150$, partial $\eta^2 = .112$), such that N1 negativity was enhanced in younger individuals with ASD compared to younger controls, no significant condition (*younger* $F_{(1,17)} = 3.30$, $p = .087$, partial $\eta^2 = .162$; *older* $F_{(1,18)} = .00$, $p = .979$, partial $\eta^2 < .0001$) or group X condition interaction emerged (*younger* $F_{(1,17)} = .02$, $p = .902$, partial $\eta^2 = .001$; *older* $F_{(1,18)} = .02$, $p = .893$, partial $\eta^2 = .001$) for either age band.

N1 mean onset latency. Similarly, individuals with ASD and controls did not differ from one another in either age group (*younger* $F_{(1,17)} = 1.15$, $p = .298$, partial $\eta^2 = .063$; *older* $F_{(1,18)} = .26$, $p = .616$, partial $\eta^2 = .014$). While no condition interaction was observed (*younger* $F_{(1,17)} = .00$, $p = .944$, partial $\eta^2 < .0001$; *older* $F_{(1,18)} = .02$, $p = .894$, partial $\eta^2 = .001$), a group X condition interaction was evidenced in the younger groups (*younger* $F_{(1,17)} = 4.48$, $p = .05$, partial $\eta^2 = .209$; *older* $F_{(1,18)} = .89$, $p = .357$, partial $\eta^2 = .047$), showing that younger individuals with ASD had prolonged N1 mean onset latencies towards the KIC condition than younger controls.

Ncl mean amplitude. Finally, no group (*younger* $F_{(1,17)} = 2.61$, $p = .125$, partial $\eta^2 = .133$; *older* $F_{(1,18)} = 3.47$, $p = .079$, partial $\eta^2 = .161$), condition (*younger* $F_{(1,17)} = .85$, $p = .369$, partial $\eta^2 = .048$; *older* $F_{(1,18)} = 1.56$, $p = .228$, partial $\eta^2 = .080$), or group X condition interaction (*younger* $F_{(1,17)} = .44$, $p = .516$, partial $\eta^2 = .025$; *older* $F_{(1,18)} = 1.58$, $p = .225$, partial $\eta^2 = .081$) emerged for the conceptual N_{cl} component.

2. Parent-Child Associations.

ASD parent-child pairs. There were no significant associations between parent and child components in response to KICs ($P1_{amp}$ *estimate* = -.12, $p = .32$, $N1_{amp}$ *estimate* = -.10, $p = .69$, $N1_{lat}$ *estimate* = .11, $p = .55$, $N1_{cl}$ *estimate* = .05, $p = .73$). Similarly, no significant relationships emerged between parent and child pairs during the non-KIC scramble condition across examined components ($P1_{amp}$ *estimate* = -.12, $p = .28$, $N1_{amp}$ *estimate* = .13, $p = .61$, $N1_{lat}$ *estimate* = .08, $p = .65$, $N1_{cl}$ *estimate* = .13, $p = .30$).

Control parent-child pairs. Similar to ASD families, no parent-child associations emerged in control families for any component during the KIC condition ($P1_{amp}$ *estimate* = .07, $p = .37$, $N1_{amp}$ *estimate* = .003, $p = .98$, $N1_{lat}$ *estimate* = -.24, $p = .39$, $N1_{cl}$ *estimate* = -.03, $p = .72$). Likewise, for the non-KIC scramble condition, no parent-child relationships emerged ($P1_{amp}$ *estimate* = .04, $p = .55$, $N1_{amp}$ *estimate* = -.02, $p = .86$, $N1_{lat}$ *estimate* = -.19, $p = .32$, $N1_{cl}$ *estimate* = -.03, $p = .75$).

3. Associations with Eye Tracking.

No associations emerged between elevated global relative to local processing on a separate eye-tracking paradigm involving KICs and any components examined in the present study across proband or parent groups.

4. Associations with Clinical-Behavioral Correlates.

ASD Group. Significant positive correlations emerged between N1 mean amplitudes during the KIC condition only, and current sensory/motor behaviors in individuals with ASD on the ADI-R (r_s = .82, p < .05). Positive correlations also emerged between sensory sensitivities and sensory avoidance behaviors with less negative N_{cl} (r_s = .94, p < .0001 and r_s = .78, p < .05, respectively) during the non-KIC scramble condition. More positive P1 mean amplitude was significantly correlated with fewer sensory avoidant behaviors across both the KIC and non-KIC scramble conditions (r_ss = -.70, ps < .05). No associations emerged between ADOS total and subtotal severity scores with any component or condition (r_ss < |.32|, ps > .34).

ASD Parent Group. In the ASD parent group, significantly greater P1 mean amplitudes across both KIC and non-KIC scramble conditions positively correlated with elevated features of the broad autism phenotype (BAP) based on the BAPQ self-rating form (*Total score* r_ss > .62, ps < .01; *Aloof* r_ss > .68, ps < .05; *Rigid* r_ss > .49, ps < .05; with no differences emerging in the *pragmatic* sub-domain r_ss < .29, ps > .25). Additionally, significant negative associations emerged between elevated aloof and rigid traits on the MPAS and more negative N_{cl} mean amplitudes during the non-KIC scramble and KIC conditions, respectively (*Aloof* r_s = -.41, p < .05; *Rigid* r_s = -.39, p < .05, respectively).

Discussion

This study examined the neural correlates of global perception in individuals with ASD and their parents, compared to respective control groups. In particular, the present study utilized EEG methods to extract event-related potentials (ERPs) in response to Kanizsa Illusory Contours (KICs) and non-illusory forms, with a primary focus on early visual perceptual components across the parieto-occipital regions of the brain. Though findings revealed the expected illusory contour effect (i.e., the IC effect—greater N1 responses to KICs compared to non-KICs) emerging across all groups, the ASD group also exhibited greater negativity over the parieto-occipital regions in response to control grid images, and prolonged latencies in response to KICs, as compared to controls. Parents with and without a child with ASD, however, had expected responses across conditions and components, with no group differences emerging in these early perceptual ERP components. Some possible atypicalities in the N_{cl} component emerged in both ASD and ASD parent groups, though these did not reach significance. While parent-child analyses did not evidence familiality in ERP components, significant relationships surfaced between ERP components and clinical and sub-clinical features associated with ASD and the broad autism phenotype. Findings suggest somewhat immature KIC perception in the early visual areas in individuals with ASD, with limited evidence of perceptual disruptions in parents of individuals with ASD.

Perceptual N1 and conceptual N_{cl} closure in ASD versus controls

An expected "IC effect" (illusory contour effect) emerged in the N1 component across both proband and parent groups, such that mean N1 amplitudes were attenuated for the non-illusory figure compared to the KIC (T. S. Altschuler et al., 2014; Altschuler et al., 2012; Foxe et

al., 2005; Foxe & Simpson, 2002b; M. M. Murray & Herrmann, 2013; M. M. Murray et al., 2006; M. M. Murray et al., 2002; Stroganova, Orekhova, et al., 2007). Specifically, the IC effect represents automatic perceptual closure without reference to stored neural representations (T. S. Altschuler et al., 2014; Altschuler et al., 2012; Foxe et al., 2005; Foxe & Simpson, 2002; M. M. Murray et al., 2002) occurring over the lateral occipital complex regions of the ventral visual stream (Fiebelkorn, Foxe, Schwartz, & Molholm, 2010; M. M. Murray et al., 2002; Sehatpour et al., 2006; Sehatpour et al., 2008). Prior work has demonstrated this perceptual IC effect emerging in both typically developing children as young as 6 years (T. S. Altschuler et al., 2014; Stroganova, Orekhova, et al., 2007) and in adults (Altschuler et al., 2012; Foxe et al., 2005) in the parieto-occipital regions of the brain. Findings from the present study therefore suggest intact object processing and perceptual closure processes in all groups, with no impairments in ventral stream processes surfaces during KIC perception. Importantly, however, our finding of an appropriate IC effect in the ASD group stands in contrast with that of another study documenting an *inverted* IC effect in preschool boys with ASD (Stroganova, Orekhova, et al., 2007). In particular, their results yielded a more positive N1 *peak* amplitude in response to the KIC, but a more negative N1 peak amplitude in response to the non-illusory figure. Despite consistent findings of bilateral IC effects, this group observed differences on central to left occipital regions in ASD, and right parietal regions in controls. Discrepant findings between these studies may be partly attributable to key methodological differences, such as component measurement type (i.e., peak amplitude versus mean amplitude measurements), sample (e.g., preschoolers versus a wider age range in the present study from school-age children to adults), and statistical analyses (e.g., exploration of differences occurring in each electrode versus an average parieto-occipital EOI in the present study).

Though not statistically significant, it appears that an inverted condition effect is occurs at the N_{cl} *conceptual* phase of the waveform among individuals with ASD, while controls' N_{cl} responses were comparable in both conditions. This second conceptual phase is thought to reflect a higher order process of closure that involves a comparison to existing neural representations and semantic processing of objects in the lateral occipital areas of the ventral stream (Doniger et al., 2000; Doniger, Foxe, et al., 2001; Foxe et al., 2005; M. M. Murray et al., 2002; Sehatpour et al., 2006; Sehatpour et al., 2008). The N_{cl} has been repeatedly shown to be more apparent during objects that are closeable (i.e., the KIC in this study) versus those that are more fragmented (i.e., the non-KIC scramble in the present study), with greater negativity in response to closeable objects (Doniger et al., 2000; Doniger, Foxe, et al., 2001). Importantly, the N_{cl} has been specifically associated with *correct* boundary completion (M. M. Murray et al., 2006), and believed to reflect conceptualization of the image by tapping into stored semantic representations. In typically developing children, younger children showed larger N_{cl} magnitudes in response to the KIC compared to a non-KIC (T. S. Altschuler et al., 2014), which was not present in adulthood. Adults instead had comparable N_{cl} amplitudes across conditions, and a prominent IC effect occurring only during the perceptual phase, suggesting a protracted developmental process of perceptual closure in which automaticity increases with age. Authors therefore posited a "late-to-early consolidation model" of ventral stream object processing during development. In the present study, however, we saw an *inverted* N_{cl} response emerging in ASD, suggesting that the KIC did not elicit neural responses indicative of an existing stored neural representation for the illusory square, while the non-KIC scramble condition did. Larger N_{cl} amplitudes in the non-KIC scramble condition in ASD may signify correct boundary completion (M. M. Murray et al., 2006) at the local level, perhaps indicating that individuals with ASD

utilized local, serial processing strategies and perceived the scramble as four individual complete objects. Indeed, a recent meta-analysis of studies of local and global processing in ASD showed that individuals with ASD may demonstrate a preference for local features (Koldewyn et al., 2013; Mottron et al., 2003; Mottron et al., 1999) and that global processing takes time (Van der Hallen et al., 2015). Similar findings have been reflected in eye-tracking studies employing KICs. For instance, while no accuracy differences were observed in a task of KIC matching between ASD and controls, eye-tracking variables revealed less global and more local (i.e., more effortful) (Navon, 1977) strategies being employed by individuals with ASD (Nayar et al., 2017; Nayar, Winston, et al., in prep). That the control group in this study yielded comparable waveforms between conditions during the N_{cl} timeframe, but the expected IC effect during the perceptual phase, resembles recent work evidencing a lack of N_{cl} differences in adult controls (T. S. Altschuler et al., 2014). This implies that KIC processing in controls in the present study likely occurs primarily during the first perceptual phase, and therefore is more automatic. Given lack of statistical differences, however, future studies may further examine the N_{cl} component by manipulating the shape or contour of the KICs (T. S. Altschuler et al., 2014), as this alters the effort necessitated to close the illusory gap.

Hyperexcitability in ASD

Although the expected IC effect emerged across proband groups, responses were more negative among individuals with ASD in response to the KIC and non-KIC scramble condition compared to the control group. It is possible that, although there were no mean differences in age between groups (see *Table 1*), the composition of the control group with a larger number of younger participants (n=14 younger than 14 years) compared to the ASD group (n=7 below 14

years) may have influenced the magnitude of the N1 response. Indeed, prior work (T. S. Altschuler et al., 2014) in typically developing children has indicated smaller magnitude N1 amplitudes in 6-12-year-olds compared to adults (with adult-like ERPs observed in 13-17-year-olds). As such, the smaller N1 mean amplitudes documented in controls versus ASD in the present study may be reflective of neurodevelopmental processes more broadly. Secondary analyses investigating the effect of age on N1 amplitude differences demonstrated no significant differences in N1 amplitude between older individuals with ASD and controls, implying that the younger participants in the control group may have impacted overall findings.

It is plausible, however, that individuals with ASD in the present study exhibited hypersensitivity to visual stimulus more broadly that was captured in this early perceptual component. Our findings showed that individuals with ASD had similarly exaggerated N1 mean amplitudes in response to the grid visual control stimulus compared to control participants, and that positive associations emerged between N1 mean amplitude and elevated sensory/motor behaviors in ASD, suggesting a possible link with ASD symptom severity. As such, group differences emerging in N1 mean amplitudes across conditions provides further evidence for this neural hyperexcitability, which has been repeatedly documented in ASD (see review Takarae & Sweeney, 2017). Cortical hyperexcitability in ASD has been hypothesized to partially stem from an imbalance between glutamatergic and GABAergic neuronal activity, particularly within regions demonstrating increased local short-range over-connectivity (Di Martino et al., 2014; Peters et al., 2013; Rane et al., 2015; Vissers, Cohen, & Geurts, 2012). Evidence from mouse models of fragile X syndrome (a genetic disorder highly comorbid with ASD) has demonstrated increased N1 amplitudes (Schneider et al., 2013; Sinclair, Oranje, Razak, Siegel, & Schmid, 2017), in both mice and children demonstrating normalized ERP responses following GABA

agonists (Schneider et al., 2013), suggesting the potential role of neural hyperexcitability in atypically exaggerating amplitudes of early components. Finally, comparably heightened N1 responses observed among individuals with ASD across all stimuli may point to reduced specialization of functional networks and perceptual categorization more broadly. For example, prior work has demonstrated neural specialization and processing of faces, as demonstrated by the inversion effect (i.e., larger N170 amplitudes to inverted faces relative to upright faces) among typically developing individuals, an effect seemingly absent in individuals with ASD (J. C. McPartland et al., 2011). As indicated above, secondary, exploratory analyses revealed that only the N1 responses of younger participants with ASD were marginally more negative compared to younger control participants, suggesting that the younger participants in these groups may be driving overall findings. Together, findings suggest that while individuals with ASD (particularly those < 14 years) show no impairments in the early perceptual phase of KIC perception, they may exhibit relatively immature and likely decreased functional specialization in early visual perceptual areas of the brain. Importantly, however, exploratory analyses examining the ratio of IC difference between N1 and P1 showed no group differences, suggesting that perhaps the magnitudes of early components may have impacted amplitude means of downstream components and therefore impacted overall findings. It is important to note, however, that prior work has demonstrated that the generation of P1 and N1 are largely independent in the ventral stream and not causally related, based on evidence of attenuated P1 amplitudes but typical N1 magnitudes in schizophrenia compared to controls (Foxe et al., 2005). Additionally, the ratio of IC effect difference was larger in the control group than in the ASD group, suggesting greater modulation of activity (T. S. Altschuler et al., 2014) among controls, with relative immaturity of early phase contour integration mechanisms in ASD. Taken together,

patterns of ERP responses documented in ASD may reflect intact, but less mature early ventral stream object processing across the parieto-occipital regions of the brain.

Early sensory component P1 in ASD and controls

Based on N1 findings reflecting hyperexcitability and prior work demonstrating elevated amplitudes in early sensory processing in response to KICs (Baruth et al., 2010), lack of heightened P1 mean amplitudes in ASD compared to controls in the present study was somewhat surprising, and likely reflects differences in study design. Prior work suggests that the visual P1 over parieto-occipital areas is thought to reflect general early registration of visual stimuli (Key, Dove, & Maguire, 2005), with generators in both the ventral and dorsal streams (Heinze et al., 1994; Mangun et al., 1997; M. M. Murray, Foxe, Higgins, Javitt, et al., 2001; M. M. Murray, Foxe, Higgins, Schroeder, et al., 2001; Simpson et al., 1995). Lack of differences in the present study may therefore indicate no disturbances in early and fundamental sensory perceptual processing among those with ASD (although, greater mean P1 amplitude was correlated with fewer sensory avoidant behaviors in ASD, reflecting its association with sensory processing more broadly). In fact, prior work has revealed similar P1 amplitudes in response to a range of visual and social (i.e., faces) stimuli between individuals with ASD and typically developing peers (J. C. McPartland et al., 2011). As such, findings from this present study suggest normative registration of fundamental sensory information in ASD, with differences emerging in subsequent perceptual stages related to KIC perception. It is important to note, however, that the P1 magnitude is typically larger in younger ages and decreases dramatically with age (T. S. Altschuler et al., 2014; Brandwein et al., 2011; Gomes et al., 2001), postulated to be due to developmental changes in scalp thickness. Indeed, significant negative associations emerged

between P1 mean amplitudes and age in both groups in the present study. Though not significant, the P1 mean amplitude in our typical sample is somewhat larger in magnitude than that of the ASD sample, with the negative-going waveform not crossing at zero microvolts in the typical group (in contrast to the ASD group). It is also noteworthy that exploratory analyses of age effects results in a significantly larger P1 amplitude in younger individuals than in older individuals with ASD only (data not shown), perhaps indicating a developmental effect of hyper-responsivity. As such, lack of overall P1 amplitude differences between groups in the present study may reflect the nature of sample characteristics between groups. Future studies may incorporate larger samples across all ages in ASD, to assess the development of early sensory and perceptual visual ERP components and KIC perception.

N1 latency in ASD versus Controls

In contrast to Strogonova's group (2007) but consistent with Baruth and colleagues' (2010) findings, individuals with ASD (particularly the younger individuals) had prolonged latencies for the KIC compared to controls. The N1 onset latency is thought to reflect the timing of perceptual closure, which is specifically influenced by reduced support ratio (i.e., the percentage of real contour versus missing contour), which does not affect N1 amplitudes (Altschuler et al., 2012). In other words, the N1 latency varies inversely with support ratio, reflecting the additional time required to "close the gap" in the illusory figure, or the time required for *perceptual* (rather than conceptual) binding to occur. As such, timing differences in ASD, suggests that while they were able to perceptually bind KIC and non-illusory figures, they demonstrated a somewhat immature response trajectory when perceiving the illusory image. The N1 latency has also been shown to decrease (i.e., response becomes faster) with age (T. S.

Altschuler et al., 2014; Brandwein et al., 2011; Lippe, Roy, Perchet, & Lassonde, 2007) in the typical population, suggesting that the perceptual closure process becomes more automated with age, demonstrating consistencies with behavioral studies of KIC perception development (e.g., Nayar et al., 2015). In the present study, timing differences were especially evident for younger individuals with ASD, who showed a prolonged response to KIC perception than their matched control peers, while older participants did not. It is therefore possible that the development of ventral stream processes in ASD may be even further delayed than that of their typically developing peers.

Tying it all together

Recent work argues that the weak central coherence and enhanced perceptual functioning theories exist in a hierarchy (Simmons & Todorova, 2018; Van der Hallen et al., 2015; Van Eylen et al., 2018; Vanmarcke et al., 2017). Specifically, this hierarchy posits that individuals with ASD show less efficient (i.e., slower) early-stage processing of the Gestalt (i.e., the weak central coherence theory), which is coupled with more efficient, later-stage processing of local information (i.e., the enhanced perceptual functioning theory). The prolonged latencies to KICs during the early processing stages within the lower-visual areas (e.g., Doniger et al., 2000), and inverted, heightened (albeit non-significant) amplitudes towards non-KIC scramble in the later high-order conceptual N_{cl} phase (and therefore a reflection of more effortful, local processing towards KIC versus non-KIC; and correct boundary completion occurring in non-illusory forms) in ASD, reveal striking consistencies with this hierarchical process of perception posited to exist in ASD. The theory further posits that individuals with ASD therefore can switch faster towards a more detail-oriented perceptual style, positioning N_{cl} latencies as an important area of future

investigation in ASD. Examination of group-average waveforms indeed revealed an earlier onset of the N_{cl} components in ASD compared to controls. Because feedback and feedforward (Doniger et al., 2000; Doniger, Silipo, et al., 2001) mechanisms between ventral lower-order and higher-order visual areas are crucial for N1 and N_{cl} components in illusory contour perception, it may be that these mechanisms are altered in individuals with ASD, as this neural pattern was not apparent in controls.

Parents of individuals with ASD versus parent controls

Parent groups showed comparable ERPs across all components examined. In other words, the present results demonstrate that neural processing of basic KIC, including the IC effects in the early perceptual and late conceptual phases are largely intact in parents of individuals with ASD. These findings, though not consistent with our hypotheses, are not surprising given the subclinical nature of ASD-related traits observed in only a subset of parents of individuals with ASD and in light of prior work evidencing a lack of N_{cl} differences in response to KIC versus non-KIC figures in adults (T. S. Altschuler et al., 2014). It is also conceivable that null findings between parent groups, confer that early visual processing may not be an underlying function of the BAP. Unlike social-cognitive differences (Losh et al., 2009) and a breakdown in language processing (as documented by eye-voice coordination) (Nayar et al., 2018) that have been observed in the BAP, low-level visual processing deficits may in contrast serve as a marker more specific to ASD rather than subclinical features of the BAP. Findings therefore contribute to a growing body of literature characterizing the BAP.

Importantly, however, trends of an observed inverted N_{cl} phase in probands with ASD were also observed in ASD parents (but not in parent controls). Such a pattern suggests the

potential for parents to perhaps rely on the second conceptual more effortful phase of processing for KICs, while non-KIC contour binding was more prominent, shedding light into the familial nature of visual processing. It is possible that, like their children, parents of individuals with ASD similarly complete the boundaries in the non-KIC condition more effectively than in the KIC condition, likely reflecting a heightened reliance on local perceptual strategies. Prior behavioral studies, though insufficient, demonstrate faster latencies during a block design task reflecting more speedy local processing than parent controls (Bolte & Poustka, 2006; Briskman et al., 2001). In addition, eye-tracking patterns suggestive of elevated local attention and rigid tendencies (Nayar et al., 2018) have also been found, highlighting the tendency for ASD parents to more rapidly complete tasks utilizing local strategies than parent controls. The emergence of associations between generally larger magnitude amplitudes in P1 and N_{cl} and features of the BAP, suggests perhaps that hypersensitivity and binding processes may be related to features of the BAP. Recent findings in ASD point to the possibility for links between sensory processing in the brain and social behaviors observed in ASD (Keehn et al., 2020), with our findings suggesting that these links may extend to unaffected relatives as well. Further exploration of these observations in larger samples of parents may reveal subgroups of parents who demonstrate atypical processing of illusory figures that may mirror the atypicalities that have been observed in ASD groups.

Limitations and future directions

This study should be interpreted in light of several limitations. Although groups were well-matched in age, the wide age range (7-22 years in the control group and 9-34 years in the ASD group) included in this study have implications for developmental effects on ERP

components, particularly given known developmental changes in the typically developing populations (e.g., T. S. Altschuler et al., 2014; Brandwein et al., 2011; Lippe et al., 2007). Although sample sizes were smaller, median age split analyses demonstrated unique differences emerging within younger participants. As such, an assessment of the developmental trajectories of ERP components in ASD is warranted as these trajectories may differentially impact ASD symptomatology. Similarly, although the IC effect has been shown to be present in young children (T. S. Altschuler et al., 2014) and variability is evident across support ratios and reaction times (Altschuler et al., 2012; Shipley & Kellman, 1992), future study of support ratio effects on perceptual boundary closure is needed to shed light on the specific timing effects of global processing. Given Altschuler and colleagues' (2012) findings of prolonged latencies (i.e., slower) with decreasing support ratios, it may be that individuals with ASD or parents would show even slower binding processes. As such, it cannot be explicitly ruled out that parents of individuals with ASD do not exhibit atypicalities in early perceptual or late conceptual phases of the two-stage consolidation model. Finally, though utilization of area measures (i.e., mean amplitude and fractional area latency) is a strength of this paper, it has posed challenges for replication, but also highlights how measurement type may significantly influence findings and interpretation (Luck, 2004).

Conclusions

Taken together, findings from this study contributes to our understanding of key cognitive and neural systems affected by ASD genetic risk. In particular, findings of intact but relatively immature ventral stream processes in ASD, and lack of differences among parents of individuals with ASD highlights the need for further investigation into the pathogenesis

associated with clinical and subclinical features of ASD. Subtle, observable (though, non-significant) differences in more effortful visual conceptualization components reflected only in ASD and ASD parent groups suggests differences in strategies being utilized to close the gap in scrambled versus KIC figures (i.e., a comparative process against existing neural representations; Doniger 2000, 2001), that may run in families of ASD. Importantly, minimal group differences and lack of familiality of ERPs examined in the present study, calls into question the utility of examining ventral stream processes as a marker of ASD-risk. It may be that early non-social visual processing atypicalities are weak ASD-related biomarkers, particularly given robust social processing biomarkers identified using ERPs in previous literature (Kang et al., 2018; J. C. McPartland, 2017; J. C. McPartland et al., 2011), as well as the mounting evidence in parents of face processing as a functional biomarker of genetic risk to ASD (Dawson et al., 2005; Yucel et al., 2015). Nonetheless, methodological strengths in this study underscore the efficacy of ERP/EEG methods to investigate objective markers of genetic susceptibility in ASD, particularly given its inherent heterogeneity (Jeste & Nelson, 2009). An examination of the neural correlates of visual processing documented in this study (versus relying on behavioral indices alone) are as advantageous as they are noninvasive, objective, and relatively easy to examine across the life-span, with strong replicability opportunities that can be used to monitor the progress of intervention in individuals with ASD. Findings from this study also highlights the importance of replication and provides a foundation for future work examining biological markers in family members of individuals with ASD.

CHAPTER 5: SUMMARY

Project Goals

This dissertation utilized a multi-method approach to exploring the biological basis of visual perception and attention in autistic individuals and their biological parents. Both visual perceptual and attentional patterns in ASD and parents with and without the broad autism phenotype (BAP) using eye tracking and electrophysiological methods were examined. A primary focus of this dissertation was to characterize early visual processing and how they related to downstream clinical and sub-clinical features of the ASD phenotype. Given that successful social interactions requires the ability to integrate information from multiple environmental and sensory modalities (e.g., facial expressions, gestures, eye contact, intonation of speech, language, body language etc), it is possible that the weak central coherence (i.e., demonstrating weaknesses in processing the Gestalt, or engaging in integrative processes) and the enhanced perceptual functioning (i.e., heightened local or detail processing) theories may decrease one's ability to process a range of information in its context, thereby impacting social interactions. These theories have been extensively studied for decades, as a means to understand the underlying mechanisms related to the social-communicative and rigid/restricted behaviors evident in ASD.

However, many studies examining these theories have relied heavily on performance-based measures during tasks that inherently involve multiple sensory modalities or confer interference effects between local and global levels, which obscures the direct examination of local and/or global processing. Additionally, given that local and global processing are core strategies used to visually perceive the world, it is controversial to rely solely on performance-

based measures of accuracy and reaction time to examine these processes. As such, the application of eye tracking in the present study offered a unique contribution to the field of local/global processing in ASD and in the BAP. Finally, given distinct neural correlates of local/global processing, the application of EEG/ERP methods provided a direct examination of the cognitive mechanisms contributing the perceived behavioral phenotypes in ASD and the BAP. This dissertation therefore uniquely explored converging measures of visual processing via multiple systems of analyses, and is among the first that took a family-study approach to examining the neural basis of visual processing. As such, findings from this dissertation have the potential to contribute to large-scale investigations to identify endophenotypes in genetic and treatment studies. This dissertation identified brain-behavior pathways via in tandem application of multimodal assessments of complex phenotypes (e.g., ASD clinical and sub-clinical features) and fundamental contributing processes (e.g., visual perception/attention via eye tracking and EEG), providing the groundwork for future investigations for characterizing the underlying mechanisms contributing to clinical and sub-clinical traits related to ASD and the BAP.

Project 1 (Chapter 2)

Social attention differences, expressed through gaze patterns, have been documented in ASD, with subtle differences also reported among first-degree relatives, suggesting a shared genetic link. Findings have mostly been derived from standard eye-tracking methods (total fixation count or total fixation duration). Given the dynamics of visual attention, these standard methods may obscure subtle, yet core, differences in visual attention mechanisms, particularly those presenting sub-clinically. Project 1 applied a constellation of eye-tracking analyses to gaze

data from individuals with ASD and their parents, to identify potentially subtle and nuanced top-down social visual attentional differences.

Project 1 identified that analytic methods examining fixations over time and repeat perseverative fixations were most robust in differentiating ASD and the BAP from controls, where they evidenced increased non-social visual attention and decreased social attention over the course of the task. This study therefore highlighted the utility of applying growth curve analytic methods to examine fixations over time, and its application to studies of eye tracking more broadly, and to studies of visual social attention in ASD and the BAP more specifically. By providing a detailed examination of looking patterns over time, growth curve analyses may thus better capture the dynamic aspects of gaze that typically occurs in natural settings and which are impacted in ASD.

Additionally, this study demonstrated atypicalities in perseverative fixations in ASD and the BAP, which may importantly be tied to increased genetic liability to ASD given their documented associations with clinical-behavioral features in ASD and the BAP. Moreover, it is possible that increased perseverative fixations towards non-social information in ASD and decreased preservative fixations towards social information may stem from differences in local (i.e., detailed) and global (i.e., integrative) visual processing in ASD more broadly (Van der Hallen et al., 2015; Van Eylen et al., 2018). Individuals with ASD have been shown to demonstrate heightened local perceptual abilities (i.e., the enhanced perceptual functioning theory) which may result in a reduction in global perceptual abilities (i.e., weak central coherence theory), suggesting that they have difficulty shifting attention from local to a global level (Plaisted et al., 1999; Rinehart et al., 2000) (see also Project 2/Chapter 3). Enhanced local

perceptual abilities also may explain the tendency for individuals with ASD to more often focus on or get distracted by insignificant, non-salient details in their environment, which has been documented in both eye-tracking studies (Chawarska et al., 2012; M. Lee et al., 2019) and autobiographical accounts (e.g., Grandin, 1995). As such, it is possible that the findings documented in the present study contribute to both the social deficit and weak central coherence/enhanced perceptual functioning theories of ASD, which further highlights the strength of this dissertation, which links these theories on one large study.

Finally, although other analytic methods applied to this project showed few differences between groups—the category of the first fixation area of interest (AOI), the duration of the first fixation, the number of fixations per second, the number of fixations per second that occurred towards social versus non-social information, the percentage of refixations that occurred towards previously fixated AOIs, the percentage of fixation transitions that occurred between social and non-social information, or the percentage of area covered or attended towards social or non-social AOIs—they remain a valuable set of analytic tools that can be utilized in future studies applying eye-tracking methods, particularly as they are thought to reflect different aspects of underlying cognition (R. W. Booth & Weger, 2013; Eckstein et al., 2017; Hughes & Russell, 1993; Luna et al., 2008; Perea & Carreiras, 2003; Rayner, 1998; Rayner et al., 2010; Zagermann et al., 2018). The types of analyses utilized in this study captured the dynamic nature of gaze in contrast to average dwell time and proportion of fixation variables, which assumes a uniform or stagnant method of exploration, and tends to attenuate potential differences in looking patterns. In sum, given the objective and measurable nature of the 11 rigorous eye-tracking variables documented here, this project has the potential to serve as a proof-of-concept or a template that

could be drawn upon in future eye-tracking studies examining visual attention across other clinical and sub-clinical populations.

Project 2 (Chapter 3)

Project 2 then sought to examine local/global visual processing in autistic individuals and parents using eye tracking and performance (i.e., accuracy and reaction time) indices, with the primary goal of understanding the social-behavioral and social-communicative differences inherent to the ASD phenotype. Overall, while no significant differences emerged in performance (i.e., accuracy and reaction time measures) in ASD or ASD parent groups compared to respective controls, eye-tracking analyses revealed an overall reduced global vs. local visual processing in both groups. Findings specifically demonstrated heightened local processing (i.e., elevated rates of exploration and vacillations), in addition to reduced global perception in autistic individuals. Gaze indices that were examined as such revealed both perceptual differences as well as differences in strategies being employed to perceive local/global stimuli in ASD. In contrast, ASD parents demonstrated primarily a diminished bias towards the global percept, without indications of heightened local processing, with eye-tracking indices indicative of strategy-based differences (rather than perceptual-based differences) in global processing.

Parallel findings between ASD and ASD parent groups may therefore point to common underlying neurobiological differences in visual perception that may be a result of ASD genetic risk. Within-family similarities across ASD parent-child pairs but not in control parent-child pairs or in unrelated parent-child pairs suggests that visual processing uniquely co-segregates in ASD families, indicating potential heritability. Finally, associations between local/global

processing with elevated rates of restricted and repetitive behaviors and *better* pragmatic language abilities in ASD and ASD parents, suggests that local/global processing styles may differentially impact broader traits related to ASD. It is possible that local strategies may be helpful as an alternative strategy for tracking the details of a communication exchange. This underscores the notion that individuals with ASD, and their family members, may be using alternative strategies to achieve the same outcome as their respective controls.

Results highlight the objective and quantifiable nature of eye tracking to capture *strategies* related to local/global processing. This study also raised important questions regarding the types of stimuli utilized in prior and ongoing work of local/global processing in ASD and inform future studies to consider both perceptual and strategy-based indices to document local/global visual processing in studies of sub-clinical traits of a disorder. Eye-tracking findings documented in this project suggest that visual processing styles may be heritable, genetically meaningful features of the broader autism spectrum, thereby underscoring their utility as a candidate endophenotype.

Project 3 (Chapter 4)

Finally, project 3 explored the neural underpinnings of local/global visual processing. Atypical neural correlates of local and global processing have been identified in ASD (Baruth et al., 2010; Stroganova, Orekhova, et al., 2007), though studies had yet to investigate the underlying neurobiology of visual *perception* as a potential endophenotype among relatives, despite behavioral studies suggesting potential local/global processing differences among parents (Bolte & Poustka, 2006; Losh et al., 2009; Nayar et al., 2018; Nayar, Winston, et al., in prep).

This study implemented EEG methods to extract well-established ERPs resulting from perception of illusory contours in order to index the timing and response patterns of global perception in individuals with ASD and their parents.

Findings of atypical timing and amplitudes of ERPs in response to illusory forms to index global processing in ASD, indicate intact but relatively immature global perception in ASD, suggesting mild disruptions of ventral stream processes involved in global perception. Lack of neural differences among parents of individuals with ASD highlights the need for further investigation into the etiology associated with clinical and subclinical features of ASD. Subtle and observable differences in more effortful global perceptual processes reflected in the ERPs in ASD and ASD parent groups suggests differences in strategies utilized to close the illusory gap in the forms. Specifically, atypical patterns in more conceptual binding components in ASD and ASD parent groups suggests differences in boundary completion strategies potentially indicative of heightened local perception that may run within families of ASD. Importantly, intriguing relationships between EEG and features of the BAP emerged, perhaps implicating a link between hypersensitivity and binding processes and the BAP. These findings suggest that links between neural sensory processing and social behaviors evident in ASD may importantly extend to unaffected relatives(Keehn et al., 2020), pointing to important underlying local/global processing mechanisms contributing to the broader ASD phenotype.

Taken together, findings from this study contributes to our understanding of key cognitive and neural systems affected by ASD genetic risk, with methodological strengths underscoring the efficacy of ERP/EEG methods to investigate objective markers of genetic susceptibility in ASD. Brain-behavior relationships suggest that local/global processing

differences may be an underlying construct contributing to the already robust social processing biomarkers identified using ERPs in ASD (Kang et al., 2018; J. C. McPartland, 2017; J. C. McPartland et al., 2011) and the mounting evidence in parents of face processing as a functional biomarker of genetic risk to ASD (Dawson et al., 2005; Yucel et al., 2015). Findings from this study provides a foundation for future work examining biological markers in family members of individuals with ASD.

Across projects

Differences in local and global visual processing, as well as social and non-social visual attentional strategies, have been well documented in individuals with ASD, with findings from this dissertation further suggesting their extension to first-degree relatives with subtle features associated with ASD. In particular, findings of reduced global processing and heightened local processing were indexed via eye-tracking and electrophysiological methods in ASD. Reduced global processing was also observed among parents of individuals with ASD using eye tracking methods, with few differences emerging in their neural responses. It may be that the neural components examined in the present dissertation, which reflect early visual processing atypicalities at a fundamental level rather than at a conceptual level, may not tap the differences observed in ASD parents using eye tracking from project 2. For instance, global processing appeared to not necessarily be *impaired* in ASD parents, but rather findings suggested that they showed *reduced* global processing particularly in the face of local interference. These findings suggest that parents of individuals with ASD may utilize a different *strategy* to process information globally compared to parent controls. As such, because strategy differences are not

reflected in early ERP components examined in the present study, future studies may focus questions around later components tapping higher order skills, including an examination of fronto-temporal regions of the brain, as these areas tap higher order attentional processes that have been shown to be atypical in ASD (Baruth et al., 2010). Indeed, in project 3, observable patterns in the conceptual ERPs in both ASD and ASD parents point to potential differences in global processing conceptual strategies, and sets the ground work for future studies.

Similarly, social versus non-social visual attentional differences were documented in individuals with ASD and parents, particularly in those parents with BAP features. Findings were most apparent when examining looking patterns over the course of time, highlighting the dynamic nature of gaze that may not be captured using traditional eye-tracking methods of dwell time and percentage of fixation counts. Importantly, individuals with ASD were observed to show reduced social attention compared to controls towards the middle of the stimulus presentation, with later time-bins showing effects between BAP+ and parent control groups. It therefore becomes critical to examine timing effects in studies of visual perception and attention, particularly given delayed neural processing of KICs in individuals with documented in project 3 ASD (i.e., prolonged N1 latency to KIC), as well as prior work evidencing delayed global processing in this group (Van der Hallen et al., 2015). Findings of similar social attention at the beginning of the task, with later disengagement from social information, though speculative, suggests that perhaps individuals with ASD and parents tap local processes during social attention and global processes when examining non-social information. This may additionally explain the findings of increased local processing relating to improved pragmatic language abilities in ASD and ASD parents found in project 2. Future studies may wish to more deeply

examine timing effects of concurrent local and global processing within a framework of social and non-social visual attention. Indeed, variables tapping local perception (i.e., perseverative fixations towards non-social information) were elevated in ASD in project 1, with similar elevations observed in ASD in the percentage of vacillation and exploration during a local/global perception task in project 2.

Relatedly, while we did not observe increased rates of vacillation and exploration in parents of individuals with ASD in project 2, we did see reduced perseverative fixations towards non-social information in project 1. It is therefore possible that low-level fundamental local processing differences are not an underlying mechanism for explaining social attentional differences documented in parents in project 1 and recent literature (Adolphs et al., 2008; Bolte & Poustka, 2006; M. Lee et al., 2019; Mosconi et al., 2010; Nayar et al., 2018; Yucel et al., 2015), despite evidence suggesting that this might be the case in ASD (Behrmann et al., 2006; Burnette et al., 2005; Fitch et al., 2015; Happe, 1999; Jarrold et al., 2000; Jolliffe & Baron-Cohen, 2000; Keehn et al., 2020; Klin et al., 2002b; Van Eylen et al., 2018). Results from project 3, where no differences in neural responses to illusory forms were observed between ASD parents and parent controls, provides further evidence for this hypothesis. Finally, fewer first fixations towards target information documented in ASD parents relative to parent controls in project 2, but lack of first fixation social attention differences between groups in project 1, further suggests different mechanisms likely being tapped by local/global and visual social attentional processes in parents. Finally, given lack of differences observed neurally in ventral stream processes in project 3 in parents, and differences between parent groups observed in both global processing and social attentional *strategies* in projects 1 and 2, future studies may

examine higher-order visual processing and attentional mechanisms in the BAP; this may provide a more fruitful avenue of identifying potential biological mechanisms of perceptual and attentional atypicalities that run in families of individuals with ASD.

Taken together, global processing and social attention differences documented in projects 1 and 2 in both ASD and ASD parents (particularly in those with BAP features) using eye tracking, and differences in ventral stream processes documented using EEG in project 3, highlights the utility of applying objective methods of eye tracking and neural measures to studies of perception and attention in this population (Jeste & Nelson, 2009). Findings from this dissertation not only reveals for the first time differences in eye tracking reflecting local/global processing and social attentional looking patterns in first-degree relatives of autistic individuals, but also offers a proof-of-concept of the utility of applying objective measures of assessment to examining subtle phenotypes that may reflect an ASD-related candidate endophenotype. In sum, visual processing and attentional styles may be expressed uniquely in ASD families, that may further confer ASD genetic vulnerability.

Conclusions

Across projects, this dissertation is unique in its multidisciplinary nature, combining neuropsychological and electrophysiological neural methods with clinical-behavioral measures, within a family-genetic design. Results from this project have broad implications in their contributions not only to further characterizing the BAP, but also to our understanding of key cognitive and neural systems affected by ASD genetic risk. Additionally, results highlight the objective and quantifiable nature of eye tracking and EEG methodologies to capture *strategies*

and underlying neural mechanisms related to social attention and local/global processing. The application of a wide range of gaze analytics to eye-tracking data revealed critical temporal windows of social attentional differences in ASD and the BAP, essential for capturing subtle differences likely related to the broad ASD phenotype and contributing to social-communicative differences in ASD and the BAP. Additionally, the application of Kanizsa Illusory Contours across projects 2 and 3 are unique and critical to informing future work in ASD. The use of KICs has been extensively applied to studies of schizophrenia and typical development, particularly given their distinct neural correlates (T. S. Altschuler et al., 2014; Altschuler et al., 2012; Foxe et al., 2001; Foxe et al., 2005; Foxe & Simpson, 2002). With the addition of eye tracking in project 2, this dissertation was able to not only document reduced global processing in ASD, but also was able to demonstrate heightened local processing in the same study. As such, the use of KICs offers a unique stance in the examination of both levels of processing simultaneously without one interfering with the other, which is often the case in much of the work already conducted in ASD and confounds the examination of baseline perceptual strategies (Van der Hallen et al., 2015). Interestingly, underlying neural correlates of KICs documented in human subjects have also been extended to non-human primates (Feltner & Kiorpes, 2010; Sary et al., 2008), thus shedding light into its utility as a marker of underlying neurobiology that is devoid of culture, language, and higher cognitive abilities (unlike, for example, social stimuli). As such, KIC perception may be further examined in the context of an ASD-family study in cross-cultural work, which has the potential to span cultural boundaries to reveal a cross-cultural ASD-related endophenotype, and which may be used in future studies examining underlying neurobiological and molecular mechanisms of ASD.

This work also has implications for better understanding the biology of ASD that may lead to earlier diagnosis as well as objective measures that may be used to monitor treatment progression. The phenotypic and etiologic complexity and heterogeneity in ASD have confounded efforts to uncover the brain and gene basis of clinical features of the disorder, such as social-communicative impairments. This complexity has limited the development of targeted interventions, which have shown heterogeneous responses in ASD, likely a result of obscuring effects from the phenotypic complexity that may be detectable in more homogenous subgroups. Translational biomarkers and the multi-method deep phenotyping of visual perception and social attention documented in this dissertation can be used to stratify subgroups of individuals with more homogenous patterns of underlying visual processing and neural functioning that may contribute to outcomes or to measure treatment response to behavioral or pharmacological intervention. Subgrouping from this dissertation also has the potential to advance accurate diagnostics, clinical monitoring, as well as uncover phenotypic-genotypic expression within complex systems. Taken together, by applying this multi-method approach to deeply characterize visual perception and attention that aggregates in families and relates to other key components of the ASD phenotype, this dissertation critically informs important heritable features, and neural, biological influences underlying these profiles.

REFERENCES

Adolphs, R., Spezio, M. L., Parlier, M., & Piven, J. (2008). Distinct face-processing strategies in parents of autistic children. *Curr Biol, 18*(14), 1090-1093. doi:10.1016/j.cub.2008.06.073

Allison, T., Puce, A., Spencer, D. D., & McCarthy, G. (1999). Electrophysiological studies of human face perception. I: Potentials generated in occipitotemporal cortex by face and non-face stimuli. *Cerebral cortex, 9*(5), 415-430.

Altmann, C. F., Bulthoff, H. H., & Kourtzi, Z. (2003). Perceptual organization of local elements into global shapes in the human visual cortex. *Curr Biol, 13*(4), 342-349. doi:10.1016/s0960-9822(03)00052-6

Altschuler, E. L., Cruz, E., Salim, S. Z., Jani, J. B., Stitik, T. P., Foye, P. M., & DeLisa, J. A. (2014). Efficacy of a checklist as part of a physical medicine and rehabilitation clerkship to teach medical students musculoskeletal physical examination skills: a prospective study. *American Journal of Physical Medicine and Rehabilitation, 93*(1), 82-89. doi:10.1097/PHM.0b013e3182a92d63

Altschuler, T. S., Molholm, S., Butler, J. S., Mercier, M. R., Brandwein, A. B., & Foxe, J. J. (2014). The effort to close the gap: tracking the development of illusory contour processing from childhood to adulthood with high-density electrical mapping. *Neuroimage, 90*, 360-373. doi:10.1016/j.neuroimage.2013.12.029

Altschuler, T. S., Molholm, S., Russo, N. N., Snyder, A. C., Brandwein, A. B., Blanco, D., & Foxe, J. J. (2012). Early electrophysiological indices of illusory contour processing within the

lateral occipital complex are virtually impervious to manipulations of illusion strength. *Neuroimage, 59*(4), 4074-4085. doi:10.1016/j.neuroimage.2011.10.051

Anderson, C. J., Colombo, J., & Jill Shaddy, D. (2006). Visual scanning and pupillary responses in young children with Autism Spectrum Disorder. *J Clin Exp Neuropsychol, 28*(7), 1238-1256. doi:10.1080/13803390500376790

APA. (1994). *Publication manual of the American Psychological Association* (4th Edition ed.). Washington, DC: American Psychiatric Association.

APA. (2013). *Diagnostic and statistical manual of mental disorders (DSM-5) (5th ed.)*. Arlington, VA: American Psychiatric Association.

Au-Yeung, S. K., Benson, V., Castelhano, M., & Rayner, K. (2011). Eye movement sequences during simple versus complex information processing of scenes in autism spectrum disorder. *Autism Res Treat, 2011*, 657383. doi:10.1155/2011/657383

Awh, E., Armstrong, K. M., & Moore, T. (2006). Visual and oculomotor selection: links, causes and implications for spatial attention. *Trends Cogn Sci, 10*(3), 124-130. doi:10.1016/j.tics.2006.01.001

Bailey, A., Palferman, S., Heavey, L., & Le Couteur, A. (1998). Autism: the phenotype in relatives. *J Autism Dev Disord, 28*(5), 369-392. doi:10.1023/a:1026048320785

Bailey, A., & Parr, J. (2003). Implications of the broader phenotype for concepts of autism. *Novartis Found Symp, 251*, 26-35; discussion 36-47, 109-111, 281-197. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/14521186

Baron-Cohen, S., & Hammer, J. (1997). Parents of Children with Asperger Syndrome: What is the Cognitive Phenotype? *J Cogn Neurosci, 9*(4), 548-554. doi:10.1162/jocn.1997.9.4.548

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., & Plumb, I. (2001). The "Reading the Mind in the Eyes" Test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. *J Child Psychol Psychiatry, 42*(2), 241-251. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/11280420

Baron-Cohen, S., Wheelwright, S., & Jolliffe, T. (1997). Is there a" language of the eyes"? Evidence from normal adults, and adults with autism or Asperger syndrome. *Visual cognition, 4*(3), 311-331.

Baruth, J. M., Casanova, M. F., Sears, L., & Sokhadze, E. (2010). Early-stage visual processing abnormalities in high-functioning autism spectrum disorder (ASD). *Transl Neurosci, 1*(2), 177-187. doi:10.2478/v10134-010-0024-9

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2014). Fitting linear mixed-effects models using lme4. *arXiv preprint arXiv:1406.5823*.

Beaumont, R., & Newcombe, P. (2006). Theory of mind and central coherence in adults with high-functioning autism or Asperger syndrome. *Autism, 10*(4), 365-382. doi:10.1177/1362361306064416

Behrmann, M., Thomas, C., & Humphreys, K. (2006). Seeing it differently: visual processing in autism. *Trends Cogn Sci, 10*(6), 258-264. doi:10.1016/j.tics.2006.05.001

Benjamini, Y., & Hochberg, Y. (1995). Controlling the False Discovery Rate - a Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society Series B-Statistical Methodology, 57*(1), 289-300. doi:DOI 10.1111/j.2517-6161.1995.tb02031.x

Bertone, A., Mottron, L., Jelenic, P., & Faubert, J. (2005). Enhanced and diminished visuo-spatial information processing in autism depends on stimulus complexity. *Brain, 128*(Pt 10), 2430-2441. doi:10.1093/brain/awh561

Billeci, L., Calderoni, S., Conti, E., Gesi, C., Carmassi, C., Dell'Osso, L., . . . Guzzetta, A. (2016). The broad autism (endo)phenotype: neurostructural and neurofunctional correlates in parents of individuals with autism spectrum disorders. *Front Neurosci, 10*, 346. doi:10.3389/fnins.2016.00346

Bolte, S., Holtmann, M., Poustka, F., Scheurich, A., & Schmidt, L. (2007). Gestalt perception and local-global processing in high-functioning autism. *J Autism Dev Disord, 37*(8), 1493-1504. doi:10.1007/s10803-006-0231-x

Bolte, S., & Poustka, F. (2006). The broader cognitive phenotype of autism in parents: how specific is the tendency for local processing and executive dysfunction? *Journal of Child Psychology and Psychiatry and Allied Disciplines, 47*(6), 639-645. doi:10.1111/j.1469-7610.2006.01603.x

Booth, R., Charlton, R., Hughes, C., & Happe, F. (2003). Disentangling weak coherence and executive dysfunction: planning drawing in autism and attention-deficit/hyperactivity disorder. *Philos Trans R Soc Lond B Biol Sci, 358*(1430), 387-392. doi:10.1098/rstb.2002.1204

Booth, R. W., & Weger, U. W. (2013). The function of regressions in reading: backward eye movements allow rereading. *Mem Cognit, 41*(1), 82-97. doi:10.3758/s13421-012-0244-y

Bradshaw, J., Shic, F., Holden, A. N., Horowitz, E. J., Barrett, A. C., German, T. C., & Vernon, T. W. (2019). The use of eye tracking as a biomarker of treatment outcome in a pilot randomized clinical trial for young children with autism. *Autism Res, 12*(5), 779-793. doi:10.1002/aur.2093

Brandwein, A. B., Foxe, J. J., Russo, N. N., Altschuler, T. S., Gomes, H., & Molholm, S. (2011). The development of audiovisual multisensory integration across childhood and early adolescence: a high-density electrical mapping study. *Cereb Cortex, 21*(5), 1042-1055. doi:10.1093/cercor/bhq170

Briskman, J., Happe, F., & Frith, U. (2001). Exploring the cognitive phenotype of autism: weak "central coherence" in parents and siblings of children with autism: II. Real-life skills and preferences. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 42*(3), 309-316. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11321200

Brown, C., Gruber, T., Boucher, J., Rippon, G., & Brock, J. (2005). Gamma abnormalities during perception of illusory figures in autism. *Cortex, 41*(3), 364-376. doi:10.1016/s0010-9452(08)70273-9

Brown, C., Tollefson, N., Dunn, W., Cromwell, R., & Filion, D. (2001). The Adult Sensory Profile: measuring patterns of sensory processing. *Am J Occup Ther, 55*(1), 75-82. doi:10.5014/ajot.55.1.75

Bulf, H., Valenza, E., & Simion, F. (2009). The visual search of an illusory figure: a comparison between 6-month-old infants and adults. *Perception, 38*(9), 1313-1327. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/19911629

Bulik-Sullivan, B. K., Finucane, H. K., Anttila, V., Gusev, A., Day, F. R., Loh, P. R., . . . Nervos, G. C. A. (2015). An atlas of genetic correlations across human diseases and traits. *Nature Genetics, 47*(11), 1236-+. doi:10.1038/ng.3406

Bulik-Sullivan, B. K., Loh, P. R., Finucane, H. K., Ripke, S., Yang, J., Patterson, N., . . . Grp, S. W. (2015). LD Score regression distinguishes confounding from polygenicity in genome-wide association studies. *Nature Genetics, 47*(3), 291-+. doi:10.1038/ng.3211

Burnette, C. P., Mundy, P. C., Meyer, J. A., Sutton, S. K., Vaughan, A. E., & Charak, D. (2005). Weak central coherence and its relations to theory of mind and anxiety in autism. *J Autism Dev Disord, 35*(1), 63-73. doi:10.1007/s10803-004-1035-5

Chawarska, K., Macari, S., & Shic, F. (2012). Context modulates attention to social scenes in toddlers with autism. *J Child Psychol Psychiatry, 53*(8), 903-913. doi:10.1111/j.1469-7610.2012.02538.x

Chawarska, K., & Shic, F. (2009). Looking but not seeing: atypical visual scanning and recognition of faces in 2 and 4-year-old children with autism spectrum disorder. *J Autism Dev Disord, 39*(12), 1663-1672. doi:10.1007/s10803-009-0803-7

Chawarska, K., Volkmar, F., & Klin, A. (2010). Limited attentional bias for faces in toddlers with autism spectrum disorders. *Arch Gen Psychiatry, 67*(2), 178-185. doi:10.1001/archgenpsychiatry.2009.194

Cheung, C. H. M., Bedford, R., Johnson, M. H., Charman, T., Gliga, T., & team, B. (2018). Visual search performance in infants associates with later ASD diagnosis. *Dev Cogn Neurosci, 29*, 4-10. doi:10.1016/j.dcn.2016.09.003

Chevallier, C., Parish-Morris, J., McVey, A., Rump, K. M., Sasson, N. J., Herrington, J. D., & Schultz, R. T. (2015). Measuring social attention and motivation in autism spectrum disorder using eye-tracking: Stimulus type matters. *Autism Res, 8*(5), 620-628. doi:10.1002/aur.1479

Chita-Tegmark, M. (2016). Social attention in ASD: a review and meta-analysis of eye-tracking studies. *Res Dev Disabil, 48*, 79-93. doi:10.1016/j.ridd.2015.10.011

Chouinard, P. A., Unwin, K. L., Landry, O., & Sperandio, I. (2016a). Susceptibility to optical illusions varies as a function of the autism-spectrum quotient but not in ways predicted by

local-global biases. *J Autism Dev Disord, 46*(6), 2224-2239. doi:10.1007/s10803-016-2753-1

Clayson, P. E., Baldwin, S. A., & Larson, M. J. (2013). How does noise affect amplitude and latency measurement of event-related potentials (ERPs)? A methodological critique and simulation study. *Psychophysiology, 50*(2), 174-186.

Colombo, J., Mitchell, D. W., Coldren, J. T., & Freeseman, L. J. (1991). Individual differences in infant visual attention: are short lookers faster processors or feature processors? *Child Development, 62*(6), 1247-1257. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1786713

Constantino, J. N., & Gruber, C. (2005). *Social Responsiveness Scale*. Los Angeles: Western Psychological Services.

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

Constantino, J. N., & Todd, R. D. (2003). Autistic traits in the general population: a twin study. *Arch Gen Psychiatry, 60*(5), 524-530. doi:10.1001/archpsyc.60.5.524

Cox, M. A., Schmid, M. C., Peters, A. J., Saunders, R. C., Leopold, D. A., & Maier, A. (2013). Receptive field focus of visual area V4 neurons determines responses to illusory surfaces. *Proceedings of the National Academy of Sciences of the United States of America, 110*(42), 17095-17100. doi:10.1073/pnas.1310806110

Cribb, S. J., Olaithe, M., Di Lorenzo, R., Dunlop, P. D., & Maybery, M. T. (2016). Embedded figures test performance in the broader autism phenotype: a meta-analysis. *J Autism Dev Disord, 46*(9), 2924-2939. doi:10.1007/s10803-016-2832-3

Csibra, G., Davis, G., Spratling, M. W., & Johnson, M. H. (2000). Gamma oscillations and object processing in the infant brain. *Science, 290*(5496), 1582-1585. doi:10.1126/science.290.5496.1582

Cuccaro, M. L., Shao, Y. J., Grubber, J., Slifer, M., Wolpert, C. M., Donnelly, S. L., . . . Pericak-Vance, M. A. (2003). Factor analysis of restricted and repetitive behaviors in autism using the Autism Diagnostic Interview-R. *Child Psychiatry & Human Development, 34*(1), 3-17. doi:Doi 10.1023/A:1025321707947

Dalton, K. M., Nacewicz, B. M., Johnstone, T., Schaefer, H. S., Gernsbacher, M. A., Goldsmith, H. H., . . . Davidson, R. J. (2005). Gaze fixation and the neural circuitry of face processing in autism. *Nat Neurosci, 8*(4), 519-526. doi:10.1038/nn1421

Davidson, J., Goin-Kochel, R. P., Green-Snyder, L. A., Hundley, R. J., Warren, Z., & Peters, S. U. (2014). Expression of the broad autism phenotype in simplex autism families from the Simons Simplex Collection. *J Autism Dev Disord, 44*(10), 2392-2399. doi:10.1007/s10803-012-1492-1

Dawson, G., Webb, S. J., Wijsman, E., Schellenberg, G., Estes, A., Munson, J., & Faja, S. (2005). Neurocognitive and electrophysiological evidence of altered face processing in parents of

children with autism: implications for a model of abnormal development of social brain circuitry in autism. *Dev Psychopathol, 17*(3), 679-697. doi:10.1017/S0954579405050327

De Rubeis, S., He, X., Goldberg, A. P., Poultney, C. S., Samocha, K., Cicek, A. E., . . . Consortium, A. S. (2014). Synaptic, transcriptional and chromatin genes disrupted in autism. *Nature, 515*(7526), 209-U119. doi:10.1038/nature13772

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

Demarais, A. M., & Cohen, B. H. (1998). Evidence for image-scanning eye movements during transitive inference. *Biol Psychol, 49*(3), 229-247. doi:10.1016/s0301-0511(98)00042-8

Dennis, M., Francis, D. J., Cirino, P. T., Schachar, R., Barnes, M. A., & Fletcher, J. M. (2009). Why IQ is not a covariate in cognitive studies of neurodevelopmental disorders. *J Int Neuropsychol Soc, 15*(3), 331-343. doi:10.1017/S1355617709090481

Di Martino, A., Fair, D. A., Kelly, C., Satterthwaite, T. D., Castellanos, F. X., Thomason, M. E., . . . Milham, M. P. (2014). Unraveling the miswired connectome: a developmental perspective. *Neuron, 83*(6), 1335-1353. doi:10.1016/j.neuron.2014.08.050

DiCriscio, A. S., Hu, Y., & Troiani, V. (2019). Brief Report: Pupillometry, Visual Perception, and ASD Features in a Task-Switching Paradigm. *J Autism Dev Disord, 49*(12), 5086-5099. doi:10.1007/s10803-019-04213-8

Dink, J. W., & Ferguson, B. (2015). eyetrackingR: An R Library for Eye-tracking Data Analysis. . Retrieved from http://www.eyetrackingr.com

Doniger, G. M., Foxe, J. J., Murray, M. M., Higgins, B. A., & Javitt, D. C. (2002). Impaired visual object recognition and dorsal/ventral stream interaction in schizophrenia. *Arch Gen Psychiatry, 59*(11), 1011-1020. doi:10.1001/archpsyc.59.11.1011

Doniger, G. M., Foxe, J. J., Murray, M. M., Higgins, B. A., Snodgrass, J. G., Schroeder, C. E., & Javitt, D. C. (2000). Activation timecourse of ventral visual stream object-recognition areas: high density electrical mapping of perceptual closure processes. *J Cogn Neurosci, 12*(4), 615-621. doi:10.1162/089892900562372

Doniger, G. M., Foxe, J. J., Schroeder, C. E., Murray, M. M., Higgins, B. A., & Javitt, D. C. (2001). Visual perceptual learning in human object recognition areas: a repetition priming study using high-density electrical mapping. *Neuroimage, 13*(2), 305-313. doi:10.1006/nimg.2000.0684

Doniger, G. M., Silipo, G., Rabinowicz, E. F., Snodgrass, J. G., & Javitt, D. C. (2001). Impaired sensory processing as a basis for object-recognition deficits in schizophrenia. *Am J Psychiatry, 158*(11), 1818-1826. doi:10.1176/appi.ajp.158.11.1818

Dunn, W. (1994). Performance of typical children on the Sensory Profile: an item analysis. *Am J Occup Ther, 48*(11), 967-974. doi:10.5014/ajot.48.11.967

Eckstein, M. K., Guerra-Carrillo, B., Singley, A. T. M., & Bunge, S. A. (2017). Beyond eye gaze: What else can eyetracking reveal about cognition and cognitive development? *Developmental cognitive neuroscience, 25*, 69-91.

Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & psychophysics, 16*(1), 143-149.

Ettinger, U., Kumari, V., Crawford, T. J., Corr, P. J., Das, M., Zachariah, E., . . . Sharma, T. (2004). Smooth pursuit and antisaccade eye movements in siblings discordant for schizophrenia. *J Psychiatr Res, 38*(2), 177-184. doi:10.1016/s0022-3956(03)00105-5

Falck-Ytter, T., Fernell, E., Gillberg, C., & von Hofsten, C. (2010). Face scanning distinguishes social from communication impairments in autism. *Dev Sci, 13*(6), 864-875. doi:10.1111/j.1467-7687.2009.00942.x

Feltner, K. A., & Kiorpes, L. (2010). Global visual processing in macaques studied using Kanizsa illusory shapes. *Visual Neuroscience, 27*(3-4), 131-138. doi:10.1017/S0952523810000088

Ffytche, D. H., & Zeki, S. (1996). Brain activity related to the perception of illusory contours. *Neuroimage, 3*(2), 104-108. doi:10.1006/nimg.1996.0012

Fiebelkorn, I. C., Foxe, J. J., Schwartz, T. H., & Molholm, S. (2010). Staying within the lines: the formation of visuospatial boundaries influences multisensory feature integration. *Eur J Neurosci, 31*(10), 1737-1743. doi:10.1111/j.1460-9568.2010.07196.x

Fink, G. R., Halligan, P. W., Marshall, J. C., Frith, C. D., Frackowiak, R. S., & Dolan, R. J. (1997). Neural mechanisms involved in the processing of global and local aspects of hierarchically organized visual stimuli. *Brain, 120 (Pt 10)*, 1779-1791. doi:10.1093/brain/120.10.1779

Fischer, J., Koldewyn, K., Jiang, Y. V., & Kanwisher, N. (2014). Unimpaired Attentional Disengagement and Social Orienting in Children with Autism. *Clin Psychol Sci, 2*(2), 214-223. doi:10.1177/2167702613496242

Fitch, A., Fein, D. A., & Eigsti, I. M. (2015). Detail and gestalt focus in individuals with optimal outcomes from autism spectrum disorders. *Journal of Autism and Developmental Disorders, 45*(6), 1887-1896. doi:10.1007/s10803-014-2347-8

Foxe, J. J., Doniger, G. M., & Javitt, D. C. (2001). Early visual processing deficits in schizophrenia: impaired P1 generation revealed by high-density electrical mapping. *Neuroreport, 12*(17), 3815-3820. doi:10.1097/00001756-200112040-00043

Foxe, J. J., Murray, M. M., & Javitt, D. C. (2005). Filling-in in schizophrenia: a high-density electrical mapping and source-analysis investigation of illusory contour processing. *Cereb Cortex, 15*(12), 1914-1927. doi:10.1093/cercor/bhi069

Foxe, J. J., & Simpson, G. V. (2002). Flow of activation from V1 to frontal cortex in humans. A framework for defining "early" visual processing. *Exp Brain Res, 142*(1), 139-150. doi:10.1007/s00221-001-0906-7

Franchini, M., Glaser, B., de Wilde, H. W., Gentaz, E., Eliez, S., & Schaer, M. (2017). Social orienting and joint attention in preschoolers with autism spectrum disorders. *PLoS One, 12*(6). doi:ARTN e0178859

10.1371/journal.pone.0178859

Frazier, T. W., Strauss, M., Klingemier, E. W., Zetzer, E. E., Hardan, A. Y., Eng, C., & Youngstrom, E. A. (2017). A meta-analysis of gaze differences to social and nonsocial information between individuals with and without autism. *J Am Acad Child Adolesc Psychiatry, 56*(7), 546-555. doi:10.1016/j.jaac.2017.05.005

Freeseman, L. J., Colombo, J., & Coldren, J. T. (1993). Individual differences in infant visual attention: four-month-olds' discrimination and generalization of global and local stimulus properties. *Child Dev, 64*(4), 1191-1203. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/8404264

Frith, U. (1989). A new look at language and communication in autism. *Br J Disord Commun, 24*(2), 123-150. doi:10.3109/13682828909011952

Frith, U., & Happe, F. (1994). Autism: beyond "theory of mind". *Cognition, 50*(1-3), 115-132. doi:10.1016/0010-0277(94)90024-8

Gauglerl, T., Klei, L., Sanders, S. J., Bodea, C. A., Goldberg, A. P., Lee, A. B., . . . Buxbaum, J. D. (2014). Most genetic risk for autism resides with common variation. *Nature Genetics, 46*(8), 881-885. doi:10.1038/ng.3039

Gioia, G. A., Isquith, P. K., Guy, S. C., & Kenworthy, L. (2000). *Behavior rating inventory of executive function: BRIEF*: Psychological Assessment Resources Odessa, FL.

Gomes, H., Dunn, M., Ritter, W., Kurtzberg, D., Brattson, A., Kreuzer, J. A., & Vaughan, H. G., Jr. (2001). Spatiotemporal maturation of the central and lateral N1 components to tones. *Brain Res Dev Brain Res, 129*(2), 147-155. doi:10.1016/s0165-3806(01)00196-1

Gotham, K., Pickles, A., & Lord, C. (2009). Standardizing ADOS scores for a measure of severity in autism spectrum disorders. *J Autism Dev Disord, 39*(5), 693-705. doi:10.1007/s10803-008-0674-3

Gottesman, I. I., & Gould, T. D. (2003). The endophenotype concept in psychiatry: etymology and strategic intentions. *Am J Psychiatry, 160*(4), 636-645. doi:10.1176/appi.ajp.160.4.636

Grandin, T. (1995). Thinking in pictures and other reports from my life with autism.

Grice, S. J., Haan, M. D., Halit, H., Johnson, M. H., Csibra, G., Grant, J., & Karmiloff-Smith, A. (2003). ERP abnormalities of illusory contour perception in Williams syndrome. *Neuroreport, 14*(14), 1773-1777. doi:10.1097/00001756-200310060-00003

Groen, W. B., Rommelse, N., de Wit, T., Zwiers, M. P., van Meerendonck, D., van der Gaag, R. J., & Buitelaar, J. K. (2012). Visual scanning in very young children with autism and their unaffected parents. *Autism Res Treat, 2012*, 748467. doi:10.1155/2012/748467

Grosbras, M. H., Laird, A. R., & Paus, T. (2005). Cortical regions involved in eye movements, shifts of attention, and gaze perception. *Hum Brain Mapp, 25*(1), 140-154. doi:10.1002/hbm.20145

Guttman, S. E., & Kellman, P. J. (2004). Contour interpolation revealed by a dot localization paradigm. *Vision Res, 44*(15), 1799-1815. doi:10.1016/j.visres.2004.02.008

Happe, F. (1996). Studying weak central coherence at low levels: children with autism do not succumb to visual illusions. A research note. *J Child Psychol Psychiatry, 37*(7), 873-877. doi:10.1111/j.1469-7610.1996.tb01483.x

Happe, F. (1999). Autism: cognitive deficit or cognitive style? *Trends Cogn Sci, 3*(6), 216-222. doi:10.1016/s1364-6613(99)01318-2

Happé, F. (2000). Parts and wholes, meaning and minds: Central coherence and its relation to theory of mind. In S. Baron-Cohen, H. Tager-Flusberg, & D. J. Cohen (Eds.), *Understanding other minds: Perspectives from developmental cognitive neuroscience* (pp. 203–221): Oxford University Press.

Happe, F., Briskman, J., & Frith, U. (2001). Exploring the cognitive phenotype of autism: weak "central coherence" in parents and siblings of children with autism: I. Experimental tests. *J Child Psychol Psychiatry, 42*(3), 299-307. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/11321199

Happe, F., & Frith, U. (2006). The weak coherence account: detail-focused cognitive style in autism spectrum disorders. *J Autism Dev Disord, 36*(1), 5-25. doi:10.1007/s10803-005-0039-0

Happe, F., Ronald, A., & Plomin, R. (2006). Time to give up on a single explanation for autism. *Nat Neurosci, 9*(10), 1218-1220. doi:10.1038/nn1770

Harris, J. J., Schwarzkopf, D. S., Song, C., Bahrami, B., & Rees, G. (2011). Contextual illusions reveal the limit of unconscious visual processing. *Psychol Sci, 22*(3), 399-405. doi:10.1177/0956797611399293

Harrop, C., Jones, D., Zheng, S., Nowell, S., Boyd, B. A., & Sasson, N. (2018). Circumscribed interests and attention in autism: the role of biological sex. *J Autism Dev Disord, 48*(10), 3449-3459. doi:10.1007/s10803-018-3612-z

Hayward, D. A., Fenerci, C., & Ristic, J. (2018). An investigation of global-local processing bias in a large sample of typical individuals varying in autism traits. *Conscious Cogn, 65*, 271-279. doi:10.1016/j.concog.2018.09.002

Heinze, H. J., Hinrichs, H., Scholz, M., Burchert, W., & Mangun, G. R. (1998). Neural mechanisms of global and local processing. A combined PET and ERP study. *J Cogn Neurosci, 10*(4), 485-498. doi:10.1162/089892998562898

Heinze, H. J., Mangun, G. R., Burchert, W., Hinrichs, H., Scholz, M., Munte, T. F., . . . et al. (1994). Combined spatial and temporal imaging of brain activity during visual selective attention in humans. *Nature, 372*(6506), 543-546. doi:10.1038/372543a0

Herrmann, C. S., & Bosch, V. (2001). Gestalt perception modulates early visual processing. *Neuroreport, 12*(5), 901-904. doi:10.1097/00001756-200104170-00007

Herrmann, C. S., & Mecklinger, A. (2001). Gamma activity in human EEG is related to highspeed memory comparisons during object selective attention. *Visual Cognition, 8*(3-5), 593-608. doi:Doi 10.1080/13506280143000142

Herrmann, C. S., Mecklinger, A., & Pfeifer, E. (1999). Gamma responses and ERPs in a visual classification task. *Clin Neurophysiol, 110*(4), 636-642. doi:10.1016/s1388-2457(99)00002-4

Herrmann, C. S., Munk, M. H., & Engel, A. K. (2004). Cognitive functions of gamma-band activity: memory match and utilization. *Trends Cogn Sci, 8*(8), 347-355. doi:10.1016/j.tics.2004.06.006

Herrmann, M. J., Ehlis, A. C., Ellgring, H., & Fallgatter, A. J. (2005). Early stages (P100) of face perception in humans as measured with event-related potentials (ERPs). *Journal of Neural Transmission, 112*(8), 1073-1081. doi:10.1007/s00702-004-0250-8

Hessels, R. S., Kemner, C., van den Boomen, C., & Hooge, I. T. (2016). The area-of-interest problem in eyetracking research: A noise-robust solution for face and sparse stimuli. *Behav Res Methods, 48*(4), 1694-1712. doi:10.3758/s13428-015-0676-y

Hiraishi, H., Haida, M., Matsumoto, M., Hayakawa, N., Inomata, S., & Matsumoto, H. (2012). Differences of prefrontal cortex activity between picture-based personality tests: a near-

infrared spectroscopy study. *J Pers Assess, 94*(4), 366-371. doi:10.1080/00223891.2012.666597

Hirsch, J., DeLaPaz, R. L., Relkin, N. R., Victor, J., Kim, K., Li, T., . . . Shapley, R. (1995). Illusory contours activate specific regions in human visual cortex: evidence from functional magnetic resonance imaging. *Proceedings of the National Academy of Sciences of the United States of America, 92*(14), 6469-6473. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/7604015

Hogan-Brown, A. L., Hoedemaker, R. S., Gordon, P. C., & Losh, M. (2014). Eye-voice span during rapid automatized naming: evidence of reduced automaticity in individuals with autism spectrum disorder and their siblings. *J Neurodev Disord, 6*(1), 33. doi:10.1186/1866-1955-6-33

Holmqvist, K., Nyström, M., Andersson, R., Dewhurst, R., Jarodzka, H., & Weijer, J. V. D. (2011). *A comprehensive guide to methods and measure*. Oxford, U: Oxford University Press.

Hughes, C., & Russell, J. (1993). Autistic children's difficulty with mental disengagement from an object: Its implications for theories of autism. *Developmental psychology, 29*(3), 498.

Hurley, R. S., Losh, M., Parlier, M., Reznick, J. S., & Piven, J. (2007). The broad autism phenotype questionnaire. *J Autism Dev Disord, 37*(9), 1679-1690. doi:10.1007/s10803-006-0299-3

Hus, V., & Lord, C. (2014). The Autism Diagnostic Observation Schedule, Module 4: Revised Algorithm and Standardized Severity Scores. *Journal of autism and developmental disorders, 44*(8), 1996-2012. doi:10.1007/s10803-014-2080-3

Iossifov, I., O'Roak, B. J., Sanders, S. J., Ronemus, M., Krumm, N., Levy, D., . . . Wigler, M. (2014). The contribution of de novo coding mutations to autism spectrum disorder. *Nature, 515*(7526), 216-U136. doi:10.1038/nature13908

Isaev, D. Y., Major, S., Murias, M., Carpenter, K. L. H., Carlson, D., Sapiro, G., & Dawson, G. (2020). Relative average look duration and its association with neurophysiological activity in young children with autism spectrum disorder. *Scientific Reports, 10*(1), 1-11.

Jarrold, C., Butler, D. W., Cottington, E. M., & Jimenez, F. (2000). Linking theory of mind and central coherence bias in autism and in the general population. *Dev Psychol, 36*(1), 126-138.

Jeste, S. S., & Nelson, C. A., 3rd. (2009). Event related potentials in the understanding of autism spectrum disorders: an analytical review. *J Autism Dev Disord, 39*(3), 495-510. doi:10.1007/s10803-008-0652-9

Jolliffe, T., & Baron-Cohen, S. (1997). Are people with autism and Asperger syndrome faster than normal on the Embedded Figures Test? *J Child Psychol Psychiatry, 38*(5), 527-534. doi:10.1111/j.1469-7610.1997.tb01539.x

Jolliffe, T., & Baron-Cohen, S. (2000). Linguistic processing in high-functioning adults with autism or Asperger's syndrome. Is global coherence impaired? *Psychol Med, 30*(5), 1169-1187. doi:10.1017/s003329179900241x

Jones, W., Carr, K., & Klin, A. (2008). Absence of preferential looking to the eyes of approaching adults predicts level of social disability in 2-year-old toddlers with autism spectrum disorder. *Arch Gen Psychiatry, 65*(8), 946-954. doi:10.1001/archpsyc.65.8.946

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

Joseph, R. M., Keehn, B., Connolly, C., Wolfe, J. M., & Horowitz, T. S. (2009). Why is visual search superior in autism spectrum disorder? *Dev Sci, 12*(6), 1083-1096. doi:10.1111/j.1467-7687.2009.00855.x

Just, M. A., & Carpenter, P. A. (1975). Eye fixations and cognitive processes.

Kang, E., Keifer, C. M., Levy, E. J., Foss-Feig, J. H., McPartland, J. C., & Lerner, M. D. (2018). Atypicality of the N170 event-related potential in autism spectrum disorder: a meta-analysis. *Biol Psychiatry Cogn Neurosci Neuroimaging, 3*(8), 657-666. doi:10.1016/j.bpsc.2017.11.003

Kanizsa, G. (1976). Subjective contours. *Sci Am, 234*(4), 48-52. doi:10.1038/scientificamerican0476-48

Kanner, L. (1943). Autistic disturbances of affective contact. *Nervous child, 2*(3), 217-250.

Kappenman, E. S., & Luck, S. J. (2010). The effects of electrode impedance on data quality and statistical significance in ERP recordings. *Psychophysiology, 47*(5), 888-904.

Katagiri, M., Kasai, T., Kamio, Y., & Murohashi, H. (2013). Individuals with Asperger's disorder exhibit difficulty in switching attention from a local level to a global level. *J Autism Dev Disord, 43*(2), 395-403. doi:10.1007/s10803-012-1578-9

Keane, B. P., Joseph, J., & Silverstein, S. M. (2014). Late, not early, stages of Kanizsa shape perception are compromised in schizophrenia. *Neuropsychologia, 56*, 302-311. doi:10.1016/j.neuropsychologia.2014.02.001

Keehn, R. J. J., Pueschel, E. B., Gao, Y., Jahedi, A., Alemu, K., Carper, R., . . . Müller, R. A. (2020). Underconnectivity between visual and salience networks and links with sensory abnormalities in autism spectrum disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*.

Kemner, C., van Ewijk, L., van Engeland, H., & Hooge, I. (2008). Brief report: eye movements during visual search tasks indicate enhanced stimulus discriminability in subjects with PDD. *J Autism Dev Disord, 38*(3), 553-557. doi:10.1007/s10803-007-0406-0

Key, A. P., Dove, G. O., & Maguire, M. J. (2005). Linking brainwaves to the brain: an ERP primer. *Dev Neuropsychol, 27*(2), 183-215. doi:10.1207/s15326942dn2702_1

Kimchi, R. (1992). Primacy of wholistic processing and global/local paradigm: a critical review. *Psychol Bull, 112*(1), 24-38. doi:10.1037/0033-2909.112.1.24

Kleinhans, N. M., Richards, T., Sterling, L., Stegbauer, K. C., Mahurin, R., Johnson, L. C., . . . Aylward, E. (2008). Abnormal functional connectivity in autism spectrum disorders during face processing. *Brain, 131*(Pt 4), 1000-1012. doi:10.1093/brain/awm334

Klin, A., & Jones, W. (2008). Altered face scanning and impaired recognition of biological motion in a 15-month-old infant with autism. *Dev Sci, 11*(1), 40-46. doi:10.1111/j.1467-7687.2007.00608.x

Klin, A., Jones, W., Schultz, R., Volkmar, F., & Cohen, D. (2002a). Defining and quantifying the social phenotype in autism. *Am J Psychiatry, 159*(6), 895-908. doi:10.1176/appi.ajp.159.6.895

Klin, A., Jones, W., Schultz, R., Volkmar, F., & Cohen, D. (2002b). Visual fixation patterns during viewing of naturalistic social situations as predictors of social competence in individuals with autism. *Arch Gen Psychiatry, 59*(9), 809-816. doi:10.1001/archpsyc.59.9.809

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

Knebel, J. F., Javitt, D. C., & Murray, M. M. (2011). Impaired early visual response modulations to spatial information in chronic schizophrenia. *Psychiatry Res, 193*(3), 168-176. doi:10.1016/j.pscychresns.2011.02.006

Knoth, I. S., Vannasing, P., Major, P., Michaud, J. L., & Lippe, S. (2014). Alterations of visual and auditory evoked potentials in fragile X syndrome. *Int J Dev Neurosci, 36*, 90-97. doi:10.1016/j.ijdevneu.2014.05.003

Koegel, R. L., & Covert, A. (1972). The relationship of self-stimulation to learning in autistic children. *Journal of Applied Behavior Analysis, 5*(4), 381-387. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16795362

Koldewyn, K., Jiang, Y. V., Weigelt, S., & Kanwisher, N. (2013). Global/local processing in autism: not a disability, but a disinclination. *J Autism Dev Disord, 43*(10), 2329-2340. doi:10.1007/s10803-013-1777-z

Kovacs, I. (1996). Gestalten of today: early processing of visual contours and surfaces. *Behav Brain Res, 82*(1), 1-11. doi:10.1016/s0166-4328(97)81103-5

Kropotov, J. D., Mueller, A., & Ponomarev, V. A. (2011). ERP-Based Endophenotypes: Application in Diagnosis and Neurotherapy. *Neurofeedback and Neuromodulation Techniques and Applications*, 47-77. doi:10.1016/B978-0-12-382235-2.00003-2

Kruggel, F., Herrmann, C. S., Wiggins, C. J., & von Cramon, D. Y. (2001). Hemodynamic and electroencephalographic responses to illusory figures: recording of the evoked potentials during functional MRI. *Neuroimage, 14*(6), 1327-1336. doi:10.1006/nimg.2001.0948

Lam, K. S., & Aman, M. G. (2007). The Repetitive Behavior Scale-Revised: independent validation in individuals with autism spectrum disorders. *J Autism Dev Disord, 37*(5), 855-866. doi:10.1007/s10803-006-0213-z

Lam, K. S. L., Bodfish, J. W., & Piven, J. (2008). Evidence for three subtypes of repetitive behavior in autism that differ in familiality and association with other symptoms. *Journal of Child Psychology and Psychiatry, 49*(11), 1193-1200.

Lamb, M. R., & Robertson, L. C. (1989). Do Response-Time Advantage and Interference Reflect the Order of Processing of Global-Level and Local-Level Information. *Perception & psychophysics, 46*(3), 254-258. doi:Doi 10.3758/Bf03208087

Landa, R. (2011). *The Pragmatic Rating Scale for School-Age Children (PRS-SA)*. Unpublished manual.

Landa, R., Piven, J., Wzorek, M. M., Gayle, J. O., Chase, G. A., & Folstein, S. E. (1992). Social language use in parents of autistic individuals. *Psychol Med, 22*(1), 245-254. doi:10.1017/s0033291700032918

Landa, R. J. (2018). Efficacy of early interventions for infants and young children with, and at risk for, autism spectrum disorders. *International Review of Psychiatry, 30*(1), 25-39. doi:10.1080/09540261.2018.1432574

Le Couteur, A., Bailey, A., Goode, S., Pickles, A., Robertson, S., Gottesman, I., & Rutter, M. (1996). A broader phenotype of autism: the clinical spectrum in twins. *J Child Psychol Psychiatry, 37*(7), 785-801. doi:10.1111/j.1469-7610.1996.tb01475.x

Lee, M., Martin, G. E., Hogan, A., Hano, D., Gordon, P. C., & Losh, M. (2018). What's the story? A computational analysis of narrative competence in autism. *Autism, 22*(3), 335-344. doi:10.1177/1362361316677957

Lee, M., Nayar, K., Maltman, N., Hamburger, D., Martin, G. E., Gordon, P. C., & Losh, M. (2019). Understanding social communication differences in autism spectrum disorder and first-

degree relatives: a study of looking and speaking. *J Autism Dev Disord*. doi:10.1007/s10803-019-03969-3

Lee, T. S., & Nguyen, M. (2001). Dynamics of subjective contour formation in the early visual cortex. *Proc Natl Acad Sci U S A, 98*(4), 1907-1911. doi:10.1073/pnas.031579998

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

Lippe, S., Roy, M. S., Perchet, C., & Lassonde, M. (2007). Electrophysiological markers of visuocortical development. *Cereb Cortex, 17*(1), 100-107. doi:10.1093/cercor/bhj130

Lopez-Calderon, J., & Luck, S. J. (2014). ERPLAB: an open-source toolbox for the analysis of event-related potentials. *Front Hum Neurosci, 8*, 213. doi:10.3389/fnhum.2014.00213

Lord, C., Risi, S., Lambrecht, L., Cook, E. H., Leventhal, B. L., DiLavore, P. C., . . . Rutter, M. (2000). The Autism Diagnostic Observation Schedule-Generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders, 30*(3), 205-223. doi:Doi 10.1023/A:1005592401947

Lord, C., Rutter, M., DiLavore, P., Risi, S., Gotham, K., & Bishop, S. (2012). Autism diagnostic observation schedule–2nd edition (ADOS-2). *Los Angeles, CA: Western Psychological Corporation*.

Lord, C., Rutter, M., & Le Couteur, A. (1994). Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 24*(5), 659-685.

Losh, M. (2011). The broad autism phenotype. In *Autism spectrum disorders*: Oxford University Press.

Losh, M., Adolphs, R., & Piven, J. (2011). The broad autism phenotype. In *Autism spectrum disorders*: Oxford University Press.

Losh, M., Adolphs, R., Poe, M. D., Couture, S., Penn, D., Baranek, G. T., & Piven, J. (2009). Neuropsychological profile of autism and the broad autism phenotype. *Arch Gen Psychiatry, 66*(5), 518-526. doi:10.1001/archgenpsychiatry.2009.34

Losh, M., Childress, D., Lam, K., & Piven, J. (2008). Defining key features of the broad autism phenotype: a comparison across parents of multiple- and single-incidence autism families. *Am J Med Genet B Neuropsychiatr Genet, 147B*(4), 424-433. doi:10.1002/ajmg.b.30612

Losh, M., Esserman, D., & Piven, J. (2010). Rapid automatized naming as an index of genetic liability to autism. *J Neurodev Disord, 2*(2), 109-116. doi:10.1007/s11689-010-9045-4

Losh, M., Klusek, J., Martin, G. E., Sideris, J., Parlier, M., & Piven, J. (2012). Defining genetically meaningful language and personality traits in relatives of individuals with fragile X syndrome and relatives of individuals with autism. *Am J Med Genet B Neuropsychiatr Genet, 159B*(6), 660-668. doi:10.1002/ajmg.b.32070

Losh, M., & Piven, J. (2007). Social-cognition and the broad autism phenotype: identifying genetically meaningful phenotypes. *J Child Psychol Psychiatry, 48*(1), 105-112. doi:10.1111/j.1469-7610.2006.01594.x

Luck, S. J. (2004). Ten simple rules for designing and interpreting ERP experiments.[In:] Event-Related Potentials: A Methods Handbook. *Handy, TC (Ed.)*.

Luck, S. J. (2014a). A closer look at ERPs and ERP components. In *An introduction to the event-related potential technique* (pp. 49-98). Cambridge, MA: MIT Press.

Luck, S. J. (2014b). *An introduction to the event-related potential technique*: MIT press.

Luck, S. J. (2014c). Quantifying ERP amplitudes and latencies. In *An introduction to the event-related potential technique*. Cambridge, MA: MIT Press.

Luck, S. J., & Kappenman, E. S. (2018, August 01, 2018). ERP Boot Camp Tip: Why mean amplitude is usually superior to peak amplitude. *Virtual ERP Boot Camp.* Retrieved from https://erpinfo.org/blog/2018/7/5/mean-versus-peak-amplitude

Luck, S. J., Lopez-Calderon, J., Huang, S., Arita, J., & Foo, E. (2017, Jan 20, 2017). ERPLAB TOOLBOX TUTORIAL. Version 6.1. Retrieved from https://github.com/lucklab/erplab.wiki.git

Luna, B., Velanova, K., & Geier, C. F. (2008). Development of eye-movement control. *Brain Cogn, 68*(3), 293-308. doi:10.1016/j.bandc.2008.08.019

Maertens, M., & Pollmann, S. (2005). fMRI reveals a common neural substrate of illusory and real contours in V1 after perceptual learning. *J Cogn Neurosci, 17*(10), 1553-1564. doi:10.1162/089892905774597209

Mangun, G. R., Hopfinger, J. B., Kussmaul, C. L., Fletcher, E. M., & Heinze, H. J. (1997). Covariations in ERP and PET measures of spatial selective attention in human extrastriate visual cortex. *Hum Brain Mapp, 5*(4), 273-279. doi:10.1002/(SICI)1097-0193(1997)5:4<273::AID-HBM12>3.0.CO;2-F

Marco, E. J., Hinkley, L. B., Hill, S. S., & Nagarajan, S. S. (2011). Sensory processing in autism: a review of neurophysiologic findings. *Pediatr Res, 69*(5 Pt 2), 48R-54R. doi:10.1203/PDR.0b013e3182130c54

Martin, I., & McDonald, S. (2003). Weak coherence, no theory of mind, or executive dysfunction? Solving the puzzle of pragmatic language disorders. *Brain and Language, 85*(3), 451-466. doi:10.1016/S0093-934x(03)00070-1

MATLAB. (2010). *version 9.6.0.1214997 (R2019a)*. Natick, Massachusetts: The MathWorks Inc.

McPartland, J., Dawson, G., Webb, S. J., Panagiotides, H., & Carver, L. J. (2004). Event-related brain potentials reveal anomalies in temporal processing of faces in autism spectrum disorder. *J Child Psychol Psychiatry, 45*(7), 1235-1245. doi:10.1111/j.1469-7610.2004.00318.x

McPartland, J. C. (2017). Developing clinically practicable biomarkers for autism spectrum disorder. *J Autism Dev Disord, 47*(9), 2935-2937. doi:10.1007/s10803-017-3237-7

McPartland, J. C., Webb, S. J., Keehn, B., & Dawson, G. (2011). Patterns of visual attention to faces and objects in autism spectrum disorder. *J Autism Dev Disord, 41*(2), 148-157. doi:10.1007/s10803-010-1033-8

Mehdizadehfar, V., Ghassemi, F., Fallah, A., & Pouretemad, H. (2020). EEG study of facial emotion recognition in the fathers of autistic children. *Biomedical Signal Processing and Control, 56*, 101721.

Milne, E., & Scope, A. (2008). Are children with autistic spectrum disorders susceptible to contour illusions? *British Journal of Developmental Psychology, 26*(1), 91-102.

Milne, E., Scope, A., Pascalis, O., Buckley, D., & Makeig, S. (2009). Independent component analysis reveals atypical electroencephalographic activity during visual perception in individuals with autism. *Biol Psychiatry, 65*(1), 22-30. doi:10.1016/j.biopsych.2008.07.017

Minshew, N. J., Goldstein, G., & Siegel, D. J. (1997). Neuropsychologic functioning in autism: profile of a complex information processing disorder. *J Int Neuropsychol Soc, 3*(4), 303-316. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/9260440

Mosconi, M. W., Kay, M., D'Cruz, A. M., Guter, S., Kapur, K., Macmillan, C., . . . Sweeney, J. A. (2010). Neurobehavioral abnormalities in first-degree relatives of individuals with autism. *Arch Gen Psychiatry, 67*(8), 830-840. doi:10.1001/archgenpsychiatry.2010.87

Mottron, L., Burack, J. A., Iarocci, G., Belleville, S., & Enns, J. T. (2003). Locally oriented perception with intact global processing among adolescents with high-functioning autism:

evidence from multiple paradigms. *J Child Psychol Psychiatry, 44*(6), 904-913. doi:10.1111/1469-7610.00174

Mottron, L., Burack, J. A., Stauder, J. E., & Robaey, P. (1999). Perceptual processing among high-functioning persons with autism. *J Child Psychol Psychiatry, 40*(2), 203-211.

Mouchetant-Rostaing, Y., Giard, M. H., Bentin, S., Aguera, P. E., & Pernier, J. (2000). Neurophysiological correlates of face gender processing in humans. *European Journal of Neuroscience, 12*(1), 303-310.

Murias, M., Major, S., Davlantis, K., Franz, L., Harris, A., Rardin, B., . . . Dawson, G. (2018). Validation of eye-tracking measures of social attention as a potential biomarker for autism clinical trials. *Autism Res, 11*(1), 166-174. doi:10.1002/aur.1894

Murray, H. A. (1943). *Thematic apperception test*. Cambridge, MA: Harvard University Press.

Murray, M. M., Foxe, D. M., Javitt, D. C., & Foxe, J. J. (2004). Setting boundaries: brain dynamics of modal and amodal illusory shape completion in humans. *Journal of Neuroscience, 24*(31), 6898-6903. doi:10.1523/JNEUROSCI.1996-04.2004

Murray, M. M., Foxe, J. J., Higgins, B. A., Javitt, D. C., & Schroeder, C. E. (2001). Visuo-spatial neural response interactions in early cortical processing during a simple reaction time task: a high-density electrical mapping study. *Neuropsychologia, 39*(8), 828-844. doi:10.1016/s0028-3932(01)00004-5

Murray, M. M., Foxe, J. J., Higgins, B. A., Schroeder, C. E., & Javitt, D. C. (2001). Intact illusory contour processing despite diminished early visual cortical responses in schizophrenia. *J Cogn Neurosci Suppl, 104*.

Murray, M. M., & Herrmann, C. S. (2013). Illusory contours: a window onto the neurophysiology of constructing perception. *Trends Cogn Sci, 17*(9), 471-481. doi:10.1016/j.tics.2013.07.004

Murray, M. M., Imber, M. L., Javitt, D. C., & Foxe, J. J. (2006). Boundary completion is automatic and dissociable from shape discrimination. *J Neurosci, 26*(46), 12043-12054. doi:10.1523/JNEUROSCI.3225-06.2006

Murray, M. M., Wylie, G. R., Higgins, B. A., Javitt, D. C., Schroeder, C. E., & Foxe, J. J. (2002). The spatiotemporal dynamics of illusory contour processing: combined high-density electrical mapping, source analysis, and functional magnetic resonance imaging. *J Neurosci, 22*(12), 5055-5073.

Nakano, T., Tanaka, K., Endo, Y., Yamane, Y., Yamamoto, T., Nakano, Y., . . . Kitazawa, S. (2010). Atypical gaze patterns in children and adults with autism spectrum disorders dissociated from developmental changes in gaze behaviour. *Proc Biol Sci, 277*(1696), 2935-2943. doi:10.1098/rspb.2010.0587

Navab, A., Gillespie-Lynch, K., Johnson, S. P., Sigman, M., & Hutman, T. (2012). Eye-Tracking as a measure of responsiveness to joint attention in infants at risk for autism. *Infancy, 17*(4), 416-431.

Navon, D. (1977). Forest before trees: the precedence effect of global features in visual perception. *Cognitive Psychol., 7*, 476-484.

Navon, D. (1983). How many trees does it take to make a forest? *Perception, 12*(3), 239-254. doi:10.1068/p120239

Nayar, K., Franchak, J., Adolph, K., & Kiorpes, L. (2015). From local to global processing: the development of illusory contour perception. *J Exp Child Psychol, 131*, 38-55. doi:10.1016/j.jecp.2014.11.001

Nayar, K., Gordon, P. C., Martin, G. E., Hogan, A. L., La Valle, C., McKinney, W., . . . Losh, M. (2018). Links between looking and speaking in autism and first-degree relatives: insights into the expression of genetic liability to autism. *Mol Autism, 9*, 51. doi:10.1186/s13229-018-0233-5

Nayar, K., Guilfoyle, J. L., Stevens, C. J., Norton, E. S., & Losh, M. (in prep). The neurocognitive underpinnings of global perception in ASD and first-degree relatives: A neurophysiological study of illusory contour processing.

Nayar, K., Voyles, A. C., Kiorpes, L., & Di Martino, A. (2017). Global and local visual processing in autism: An objective assessment approach. *Autism Res, 10*(8), 1392-1404. doi:10.1002/aur.1782

Nayar, K., Winston, M., Stevens, C. J., & Losh, M. (in prep). Visual perception and central coherence in ASD and parents: A family genetic eye-tracking study.

Neufeld, J., Hagstrom, A., Van't Westeinde, A., Lundin, K., Cauvet, E., Willfors, C., . . . Bolte, S. (2020). Global and local visual processing in autism - a co-twin-control study. *J Child Psychol Psychiatry, 61*(4), 470-479. doi:10.1111/jcpp.13120

Nieder, A. (2002). Seeing more than meets the eye: processing of illusory contours in animals. *J Comp Physiol A Neuroethol Sens Neural Behav Physiol, 188*(4), 249-260. doi:10.1007/s00359-002-0306-x

O'Connor, K., & Kirk, I. (2008). Brief Report: Atypical Social Cognition and Social Behaviours in Autism Spectrum Disorder: A Different Way of Processing Rather than an Impairment. *Journal of autism and developmental disorders, 38*(10), 1989-1997. doi:10.1007/s10803-008-0559-5

O'Riordan, M., & Plaisted, K. (2001). Enhanced discrimination in autism. *Q J Exp Psychol A, 54*(4), 961-979. doi:10.1080/713756000

Olson, C. L. (1974). Comparative robustness of six tests in multivariate analysis of variance. *Journal of the American Statistical Association, 69*(348), 894-908.

Orekhova, E. V., Elsabbagh, M., Jones, E. J., Dawson, G., Charman, T., Johnson, M. H., & Team, B. (2014). EEG hyper-connectivity in high-risk infants is associated with later autism. *J Neurodev Disord, 6*(1), 40. doi:10.1186/1866-1955-6-40

Papagiannopoulou, E. A., Chitty, K. M., Hermens, D. F., Hickie, I. B., & Lagopoulos, J. (2014). A systematic review and meta-analysis of eye-tracking studies in children with autism spectrum disorders. *Social Neuroscience*, 1-23. doi:10.1080/17470919.2014.934966

Pellicano, E., & Burr, D. (2012). When the world becomes 'too real': a Bayesian explanation of autistic perception. *Trends Cogn Sci, 16*(10), 504-510. doi:10.1016/j.tics.2012.08.009

Pellicano, E., Maybery, M., Durkin, K., & Maley, A. (2006). Multiple cognitive capabilities/deficits in children with an autism spectrum disorder: "weak" central coherence and its relationship to theory of mind and executive control. *Dev Psychopathol, 18*(1), 77-98. doi:10.1017/S0954579406060056

Pelphrey, K. A., Sasson, N. J., Reznick, J. S., Paul, G., Goldman, B. D., & Piven, J. (2002). Visual scanning of faces in autism. *J Autism Dev Disord, 32*(4), 249-261. doi:10.1023/a:1016374617369

Perea, M., & Carreiras, M. (2003). Regressions and eye movements: where and when. *Behavioral and Brain Sciences, 26*(4), 497-497.

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

Pickles, A., Starr, E., Kazak, S., Bolton, P., Papanikolaou, K., Bailey, A., . . . Rutter, M. (2000). Variable expression of the autism broader phenotype: findings from extended pedigrees. *J Child Psychol Psychiatry, 41*(4), 491-502. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/10836679

Pierce, K., Marinero, S., Hazin, R., McKenna, B., Barnes, C. C., & Malige, A. (2016). Eye tracking reveals abnormal visual preference for geometric images as an early biomarker of an autism

spectrum disorder subtype associated with increased symptom severity. *Biol Psychiatry, 79*(8), 657-666. doi:10.1016/j.biopsych.2015.03.032

Piven, J., Gayle, J., Chase, G. A., Fink, B., Landa, R., Wzorek, M. M., & Folstein, S. E. (1990). A family history study of neuropsychiatric disorders in the adult siblings of autistic individuals. *J Am Acad Child Adolesc Psychiatry, 29*(2), 177-183. doi:10.1097/00004583-199003000-00004

Piven, J., Palmer, P., Jacobi, D., Childress, D., & Arndt, S. (1997). Broader autism phenotype: evidence from a family history study of multiple-incidence autism families. *Am J Psychiatry, 154*(2), 185-190. doi:10.1176/ajp.154.2.185

Piven, J., Palmer, P., Landa, R., Santangelo, S., Jacobi, D., & Childress, D. (1997). Personality and language characteristics in parents from multiple-incidence autism families. *Am J Med Genet, 74*(4), 398-411.

Piven, J., Wzorek, M., Landa, R., Lainhart, J., Bolton, P., Chase, G. A., & Folstein, S. (1994). Personality characteristics of the parents of autistic individuals. *Psychol Med, 24*(3), 783-795. doi:10.1017/s0033291700027938

Plaisted, K., Swettenham, J., & Rees, L. (1999). Children with autism show local precedence in a divided attention task and global precedence in a selective attention task. *J Child Psychol Psychiatry, 40*(5), 733-742. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/10433407

Poirel, N., Pineau, A., & Mellet, E. (2008). What does the nature of the stimuli tell us about the Global Precedence Effect? *Acta Psychologica, 127*(1), 1-11. doi:10.1016/j.actpsy.2006.12.001

Proverbio, A. M., & Zani, A. (2002). Electrophysiological indexes of illusory contours perception in humans. *Neuropsychologia, 40*(5), 479-491. doi:Doi 10.1016/S0028-3932(01)00135-X

Rane, P., Cochran, D., Hodge, S. M., Haselgrove, C., Kennedy, D. N., & Frazier, J. A. (2015). Connectivity in Autism: A Review of MRI Connectivity Studies. *Harv Rev Psychiatry, 23*(4), 223-244. doi:10.1097/HRP.0000000000000072

Rayner, K. (1998). Eye movements in reading and information processing: 20 years of research. *Psychol Bull, 124*(3), 372-422. doi:10.1037/0033-2909.124.3.372

Rayner, K., Slattery, T. J., & Belanger, N. N. (2010). Eye movements, the perceptual span, and reading speed. *Psychon Bull Rev, 17*(6), 834-839. doi:10.3758/PBR.17.6.834

Richler, J., Bishop, S. L., Kleinke, J. R., & Lord, C. (2007a). Restricted and repetitive behaviors in young children with autism spectrum disorders. *J Autism Dev Disord, 37*(1), 73-85. doi:10.1007/s10803-006-0332-6

Richler, J., Bishop, S. L., Kleinke, J. R., & Lord, C. (2007b). Restricted and repetitive behaviors in young children with autism spectrum disorders. *Journal of autism and developmental disorders, 37*(1), 73-85. doi:10.1007/s10803-006-0332-6

Righi, G., Tenenbaum, E. J., McCormick, C., Blossom, M., Amso, D., & Sheinkopf, S. J. (2018). Sensitivity to audio-visual synchrony and its relation to language abilities in children with and without ASD. *Autism Res, 11*(4), 645-653. doi:10.1002/aur.1918

Rinehart, N. J., Bradshaw, J. L., Moss, S. A., Brereton, A. V., & Tonge, B. J. (2000). Atypical interference of local detail on global processing in high-functioning autism and Asperger's disorder. *J Child Psychol Psychiatry, 41*(6), 769-778. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/11039689

Ringach, D. L., & Shapley, R. (1996). Spatial and temporal properties of illusory contours and amodal boundary completion. *Vision Res, 36*(19), 3037-3050. doi:10.1016/0042-6989(96)00062-4

Ritzl, A., Marshall, J. C., Weiss, P. H., Zafiris, O., Shah, N. J., Zilles, K., & Fink, G. R. (2003). Functional anatomy and differential time courses of neural processing for explicit, inferred, and illusory contours. An event-related fMRI study. *Neuroimage, 19*(4), 1567-1577. doi:10.1016/s1053-8119(03)00180-0

Roberts, M. E., Barthel, F. M., Lopez, C., Tchanturia, K., & Treasure, J. L. (2011). Development and validation of the Detail and Flexibility Questionnaire (DFlex) in eating disorders. *Eat Behav, 12*(3), 168-174. doi:10.1016/j.eatbeh.2011.04.001

Robertson, C. E., & Baron-Cohen, S. (2017). Sensory perception in autism. *Nat Rev Neurosci, 18*(11), 671-684. doi:10.1038/nrn.2017.112

Rommelse, N., Langerak, I., van der Meer, J., de Bruijn, Y., Staal, W., Oerlemans, A., & Buitelaar, J. (2015). Intelligence may moderate the cognitive profile of patients with ASD. *PLoS One, 10*(10), e0138698. doi:10.1371/journal.pone.0138698

Ropar, D., & Mitchell, P. (1999). Are individuals with autism and Asperger's syndrome susceptible to visual illusions? *J Child Psychol Psychiatry, 40*(8), 1283-1293. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/10604406

Ropar, D., & Mitchell, P. (2001). Susceptibility to illusions and performance on visuospatial tasks in individuals with autism. *J Child Psychol Psychiatry, 42*(4), 539-549. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/11383970

Roth, R. M., Lance, C. E., Isquith, P. K., Fischer, A. S., & Giancola, P. R. (2013). Confirmatory factor analysis of the Behavior Rating Inventory of Executive Function-Adult version in healthy adults and application to attention-deficit/hyperactivity disorder. *Arch Clin Neuropsychol, 28*(5), 425-434. doi:10.1093/arclin/act031

Sabatinelli, D., Fortune, E. E., Li, Q., Siddiqui, A., Krafft, C., Oliver, W. T., . . . Jeffries, J. (2011). Emotional perception: meta-analyses of face and natural scene processing. *Neuroimage, 54*(3), 2524-2533. doi:10.1016/j.neuroimage.2010.10.011

Sanders, S. J., Xin, H., Willsey, A. J., Ercan-Sencicek, A. G., Samocha, K. E., Cicek, A. E., . . . Consortium, A. S. (2015). Insights into Autism Spectrum Disorder Genomic Architecture and Biology from 71 Risk Loci. *Neuron, 87*(6), 1215-1233. doi:10.1016/j.neuron.2015.09.016

Sary, G., Koteles, K., Kaposvari, P., Lenti, L., Csifcsak, G., Franko, E., . . . Tompa, T. (2008). The representation of Kanizsa illusory contours in the monkey inferior temporal cortex. *Eur J Neurosci, 28*(10), 2137-2146. doi:10.1111/j.1460-9568.2008.06499.x

Sasson, N. J., Dichter, G. S., & Bodfish, J. W. (2012). Affective responses by adults with autism are reduced to social images but elevated to images related to circumscribed interests. *PloS One, 7*(8), e42457. doi:10.1371/journal.pone.0042457

Sasson, N. J., Lam, K. S., Childress, D., Parlier, M., Daniels, J. L., & Piven, J. (2013). The broad autism phenotype questionnaire: prevalence and diagnostic classification. *Autism Res, 6*(2), 134-143. doi:10.1002/aur.1272

Sasson, N. J., Turner-Brown, L. M., Holtzclaw, T. N., Lam, K. S., & Bodfish, J. W. (2008). Children with autism demonstrate circumscribed attention during passive viewing of complex social and nonsocial picture arrays. *Autism Res, 1*(1), 31-42. doi:10.1002/aur.4

Schneider, A., Leigh, M. J., Adams, P., Nanakul, R., Chechi, T., Olichney, J., . . . Hessl, D. (2013). Electrocortical changes associated with minocycline treatment in fragile X syndrome. *J Psychopharmacol, 27*(10), 956-963. doi:10.1177/0269881113494105

Scholte, H. S., Jolij, J., Fahrenfort, J. J., & Lamme, V. A. (2008). Feedforward and recurrent processing in scene segmentation: electroencephalography and functional magnetic resonance imaging. *Journal of Cognitive Neuroscience, 20*(11), 2097-2109. doi:10.1162/jocn.2008.20142

Schulze, K. K., Hall, M. H., McDonald, C., Marshall, N., Walshe, M., Murray, R. M., & Bramon, E. (2007). P50 auditory evoked potential suppression in bipolar disorder patients with psychotic features and their unaffected relatives. *Biological Psychiatry, 62*(2), 121-128. doi:10.1016/j.biopsych.2006.08.006

Sehatpour, P., Molholm, S., Javitt, D. C., & Foxe, J. J. (2006). Spatiotemporal dynamics of human object recognition processing: an integrated high-density electrical mapping and functional imaging study of "closure" processes. *Neuroimage, 29*(2), 605-618. doi:10.1016/j.neuroimage.2005.07.049

Sehatpour, P., Molholm, S., Schwartz, T. H., Mahoney, J. R., Mehta, A. D., Javitt, D. C., . . . Foxe, J. J. (2008). A human intracranial study of long-range oscillatory coherence across a frontal-occipital-hippocampal brain network during visual object processing. *Proc Natl Acad Sci U S A, 105*(11), 4399-4404. doi:10.1073/pnas.0708418105

Shah, A., & Frith, U. (1983). An islet of ability in autistic children: a research note. *J Child Psychol Psychiatry, 24*(4), 613-620. doi:10.1111/j.1469-7610.1983.tb00137.x

Shah, A., & Frith, U. (1993). Why do autistic individuals show superior performance on the block design task? *J Child Psychol Psychiatry, 34*(8), 1351-1364. doi:10.1111/j.1469-7610.1993.tb02095.x

Shic, F., Bradshaw, J., Klin, A., Scassellati, B., & Chawarska, K. (2011). Limited activity monitoring in toddlers with autism spectrum disorder. *Brain Res, 1380*, 246-254. doi:10.1016/j.brainres.2010.11.074

Shic, F., Chawarska, K., Bradshaw, J., & Scassellati, B. (2008) *Autism, Eye-Tracking, Entropy.*, 2008 Ieee 7th International Conference on Development and Learning.

Shic, F., Chawarska, K., & Scassellati, B. (2008a). *The Amorphous Fixation Measure Revisited: with Applications to Autism.* Paper presented at the 30th Annual Meeting of the Cognitive Science Society, Washington, DC.

Shic, F., Chawarska, K., & Scassellati, B. (2008b). *The Incomplete Fixation Measure*. Proceedings of the Eye Tracking Research and Applications Symposium (Etra 2008).

Shipley, T. F., & Kellman, P. J. (1992). Strength of visual interpolation depends on the ratio of physically specified to total edge length. *Percept Psychophys, 52*(1), 97-106. doi:10.3758/bf03206762

Shoji, H., Shinoda, H., & Ozaki, H. (2002). *The useful visual field and ERP topography in persons with intellectual disabilities.* Paper presented at the International Congress Series.

Shpaner, M., Molholm, S., Forde, E., & Foxe, J. J. (2013). Disambiguating the roles of area V1 and the lateral occipital complex (LOC) in contour integration. *Neuroimage, 69*, 146-156. doi:10.1016/j.neuroimage.2012.11.023

Shpaner, M., Murray, M. M., & Foxe, J. J. (2009). Early processing in the human lateral occipital complex is highly responsive to illusory contours but not to salient regions. *Eur J Neurosci, 30*(10), 2018-2028. doi:10.1111/j.1460-9568.2009.06981.x

Simmons, D. R., & Todorova, G. K. (2018). Local versus global processing in autism: special section editorial. *J Autism Dev Disord, 48*(4), 1338-1340. doi:10.1007/s10803-017-3452-2

Simpson, G. V., Foxe, J. J., Vaughan, H. G., Jr., Mehta, A. D., & Schroeder, C. E. (1995). Integration of electrophysiological source analyses, MRI and animal models in the study of visual processing and attention. *Electroencephalogr Clin Neurophysiol Suppl, 44*, 76-92.

Sinclair, D., Oranje, B., Razak, K. A., Siegel, S. J., & Schmid, S. (2017). Sensory processing in autism spectrum disorders and fragile X syndrome-From the clinic to animal models. *Neurosci Biobehav Rev, 76*(Pt B), 235-253. doi:10.1016/j.neubiorev.2016.05.029

Sokhadze, E., Baruth, J., Tasman, A., Sears, L., Mathai, G., El-Baz, A., & Casanova, M. F. (2009). Event-related potential study of novelty processing abnormalities in autism. *Appl Psychophysiol Biofeedback, 34*(1), 37-51. doi:10.1007/s10484-009-9074-5

Speer, L. L., Cook, A. E., McMahon, W. M., & Clark, E. (2007). Face processing in children with autism: effects of stimulus contents and type. *Autism, 11*(3), 265-277. doi:10.1177/1362361307076925

Stanley, D. A., & Rubin, N. (2003). fMRI activation in response to illusory contours and salient regions in the human lateral occipital complex. *Neuron, 37*(2), 323-331. doi:10.1016/s0896-6273(02)01148-0

Stroganova, T. A., Nygren, G., Tsetlin, M. M., Posikera, I. N., Gillberg, C., Elam, M., & Orekhova, E. V. (2007). Abnormal EEG lateralization in boys with autism. *Clin Neurophysiol, 118*(8), 1842-1854. doi:10.1016/j.clinph.2007.05.005

Stroganova, T. A., Orekhova, E. V., Prokofyev, A. O., Posikera, I. N., Morozov, A. A., Obukhov, Y. V., & Morozov, V. A. (2007). Inverted event-related potentials response to illusory contour in boys with autism. *Neuroreport, 18*(9), 931-935. doi:10.1097/WNR.0b013e32811e151b

Stroganova, T. A., Orekhova, E. V., Prokofyev, A. O., Tsetlin, M. M., Gratchev, V. V., Morozov, A. A., & Obukhov, Y. V. (2012). High-frequency oscillatory response to illusory contour in typically developing boys and boys with autism spectrum disorders. *Cortex, 48*(6), 701-717. doi:10.1016/j.cortex.2011.02.016

Sugawara, M., & Morotomi, T. (1991). Visual evoked potentials elicited by subjective contour figures. *Scand J Psychol, 32*(4), 352-357. doi:10.1111/j.1467-9450.1991.tb00886.x

Swanson, M. R., Serlin, G. C., & Siller, M. (2013). Broad autism phenotype in typically developing children predicts performance on an eye-tracking measure of joint attention. *J Autism Dev Disord, 43*(3), 707-718. doi:10.1007/s10803-012-1616-7

Takarae, Y., & Sweeney, J. (2017). Neural hyperexcitability in autism spectrum disorders. *Brain sciences, 7*(10), 129.

Tallon-Baudry, C., Bertrand, O., Wienbruch, C., Ross, B., & Pantev, C. (1997). Combined EEG and MEG recordings of visual 40 Hz responses to illusory triangles in human. *Neuroreport, 8*(5), 1103-1107. doi:10.1097/00001756-199703240-00008

Team, R. C. (2019). R: A Language and Environment for Statistical Computing. In R. F. f. S. Computing (Ed.). Vienna, Austria.

Theeuwes, J., Belopolsky, A., & Olivers, C. N. (2009). Interactions between working memory, attention and eye movements. *Acta Psychol (Amst), 132*(2), 106-114. doi:10.1016/j.actpsy.2009.01.005

Thibaut, J. P., & French, R. M. (2016). Analogical reasoning, control and executive functions: a developmental investigation with eye-tracking. *Cognitive Development, 38*, 10-26.

Thomas, L. E., & Lleras, A. (2007). Moving eyes and moving thought: on the spatial compatibility between eye movements and cognition. *Psychon Bull Rev, 14*(4), 663-668. doi:10.3758/bf03196818

Tierney, A. L., Gabard-Durnam, L., Vogel-Farley, V., Tager-Flusberg, H., & Nelson, C. A. (2012). Developmental trajectories of resting EEG power: an endophenotype of autism spectrum disorder. *PLoS One, 7*(6), e39127. doi:10.1371/journal.pone.0039127

Trujillo, L. T., Stanfield, C. T., & Vela, R. D. (2017). The effect of electroencephalogram (EEG) reference choice on information-theoretic measures of the complexity and integration of EEG signals. *Front Neurosci, 11*, 425. doi:10.3389/fnins.2017.00425

Turk, A. A., Brown, W. S., Symington, M., & Paul, L. K. (2010). Social narratives in agenesis of the corpus callosum: linguistic analysis of the Thematic Apperception Test. *Neuropsychologia, 48*(1), 43-50. doi:10.1016/j.neuropsychologia.2009.08.009

Tyrer, P. (1988). *Personality assessment schedule*. Course London: Butterworth and Company.

Ungerleider, L. G. (1982). Two cortical visual systems. *Analysis of visual behavior*, 549-586.

Unruh, K. E., Sasson, N. J., Shafer, R. L., Whitten, A., Miller, S. J., Turner-Brown, L., & Bodfish, J. W. (2016). Social orienting and attention is influenced by the presence of competing nonsocial information in adolescents with autism. *Front Neurosci, 10*, 586. doi:10.3389/fnins.2016.00586

Van der Hallen, R., Evers, K., Brewaeys, K., Van den Noortgate, W., & Wagemans, J. (2015). Global processing takes time: a meta-analysis on local-global visual processing in ASD. *Psychol Bull, 141*(3), 549-573. doi:10.1037/bul0000004

Van der Stigchel, S., Meeter, M., & Theeuwes, J. (2006). Eye movement trajectories and what they tell us. *Neurosci Biobehav Rev, 30*(5), 666-679. doi:10.1016/j.neubiorev.2005.12.001

van Dinteren, R., Arns, M., Jongsma, M. L., & Kessels, R. P. (2014). P300 development across the lifespan: a systematic review and meta-analysis. *PLoS One, 9*(2), e87347. doi:10.1371/journal.pone.0087347

Van Eylen, L., Boets, B., Cosemans, N., Peeters, H., Steyaert, J., Wagemans, J., & Noens, I. (2017). Executive functioning and local-global visual processing: candidate

endophenotypes for autism spectrum disorder? *J Child Psychol Psychiatry, 58*(3), 258-269. doi:10.1111/jcpp.12637

Van Eylen, L., Boets, B., Steyaert, J., Wagemans, J., & Noens, I. (2018). Local and Global Visual Processing in Autism Spectrum Disorders: Influence of Task and Sample Characteristics and Relation to Symptom Severity. *J Autism Dev Disord, 48*(4), 1359-1381. doi:10.1007/s10803-015-2526-2

Vanmarcke, S., Noens, I., Steyaert, J., & Wagemans, J. (2017). Spatial frequency priming of scene perception in adolescents with and without ASD. *J Autism Dev Disord, 47*(7), 2023-2038. doi:10.1007/s10803-017-3123-3

Varni, J. W., Lovaas, O. I., Koegel, R. L., & Everett, N. L. (1979). An analysis of observational learning in autistic and normal children. *Journal of Abnormal Child Psychology, 7*(1), 31-43. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/438430

Vigneau, F., Caissie, A. F., & Bors, D. A. (2006). Eye-movement analysis demonstrates strategic influences on intelligence. *Intelligence, 34*(3), 261-272.

Vissers, M. E., Cohen, M. X., & Geurts, H. M. (2012). Brain connectivity and high functioning autism: A promising path of research that needs refined models, methodological convergence, and stronger behavioral links. *Neuroscience and Biobehavioral Reviews, 36*(1), 604-625. doi:10.1016/j.neubiorev.2011.09.003

Vogel, E. K., & Luck, S. J. (2000). The visual N1 component as an index of a discrimination process. *Psychophysiology, 37*(2), 190-203.

Wang, Q., Campbell, D. J., Macari, S. L., Chawarska, K., & Shic, F. (2018). Operationalizing atypical gaze in toddlers with autism spectrum disorders: a cohesion-based approach. *Mol Autism, 9*, 25. doi:10.1186/s13229-018-0211-y

Wass, S. V., Forssman, L., & Leppänen, J. (2014). Robustness and precision: How data quality may influence key dependent variables in infant eye-tracker analyses. *Infancy, 19*(5), 427-460.

Wass, S. V., Smith, T. J., & Johnson, M. H. (2013). Parsing eye-tracking data of variable quality to provide accurate fixation duration estimates in infants and adults. *Behav Res Methods, 45*(1), 229-250. doi:10.3758/s13428-012-0245-6

Wechsler, D. (1991). Manual for the Wechsler Intelligence Scale for Children—third edition. *San Antonio, TX: The Psychological Corporation*.

Wechsler, D. (1999). *Wechsler Abbreviated Scale of Intelligence (WASI)*. New York, NY: The Psychological Corporation: Harcourt Brace & Company.

Weintraub, S., Dikmen, S. S., Heaton, R. K., Tulsky, D. S., Zelazo, P. D., Bauer, P. J., . . . Gershon, R. C. (2013). Cognition assessment using the NIH Toolbox. *Neurology, 80*(11 Suppl 3), S54-64. doi:10.1212/WNL.0b013e3182872ded

Winston, M., Nayar, K., Hogan, A. L., Barstein, J., La Valle, C., Sharp, K., . . . Losh, M. (2020). Physiological regulation and social-emotional processing in female carriers of the FMR1 premutation. *Physiology & behavior, 214*, 112746.

Wokke, M. E., Vandenbroucke, A. R., Scholte, H. S., & Lamme, V. A. (2013). Confuse your illusion: feedback to early visual cortex contributes to perceptual completion. *Psychological Science, 24*(1), 63-71. doi:10.1177/0956797612449175

Woodbury-Smith, M., Paterson, A. D., O'Connor, I., Zarrei, M., Yuen, R. K. C., Howe, J. L., . . . Szatmari, P. (2018). A genome-wide linkage study of autism spectrum disorder and the broad autism phenotype in extended pedigrees. *J Neurodev Disord, 10*(1), 20. doi:10.1186/s11689-018-9238-9

Wynn, J. K., Roach, B. J., Lee, J., Horan, W. P., Ford, J. M., Jimenez, A. M., & Green, M. F. (2015). EEG findings of reduced neural synchronization during visual integration in schizophrenia. *PLoS One, 10*(3), e0119849. doi:10.1371/journal.pone.0119849

Yarbus, A. L. (1967). Eye Movements During Perception of Complex Objects. In *Eye Movements and Vision*. New York: Plenum Press.

Yucel, G. H., Belger, A., Bizzell, J., Parlier, M., Adolphs, R., & Piven, J. (2015). Abnormal neural activation to faces in the parents of children with autism. *Cereb Cortex, 25*(12), 4653-4666. doi:10.1093/cercor/bhu147

Zagermann, J., Pfeil, U., & Reiterer, H. (2018). *Studying eye movements as a basis for measuring cognitive load.* Paper presented at the Extended Abstracts of the 2018 CHI Conference on Human Factors in Computing Systems.