THE DEVELOPMENT OF FACE PROCESSING DEFICITS IN AUTISM:

A META-ANALYTIC REVIEW

By

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Abnormal visual scanning of faces in individuals with autism is a predictor and possible precursor to more prominent social communication deficits seen in autism (Klin et al., 2002; Sasson, 2006) and it is one of the earliest symptoms (Dawson et al., 2005). The aim of the present meta-analysis is to determine the degree and significance of differences in looking behaviors between infants at high and low risk of autism, and to examine if these differences are affected by the type of social stimuli used. High and low risk infants' looking behaviors were compared when viewing static and dynamic stimuli and when participating in the still-face paradigm. Studies were included if they utilized infants (birth to 12 months) both at high risk and low risk for developing autism and used an eye-tracker to measure duration of time looking at facial stimuli. Twenty-one studies met inclusion criteria. The overall effect size of differences in looking behaviors for high and low risk infants was 0.03 (95% -0.06 – 0.12). There were no significant effects of age, gender, or type of stimulus on infants' looking behaviors. While majority of studies found an effect in the difference of looking behaviors between infants at high and low risk, the inconsistency of the combined results resulted in an overall nonsignificant effect size. These findings indicate reduced eye contact may not be as reliable of a behavioral marker within the first year of life as previous research has indicated.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER I: INTRODUCTION

Autism Spectrum Disorder (ASD) is a pervasive neurodevelopmental disorder, in which symptoms begin before the age of 3-years-old and persist throughout adolescence and into adulthood. One in 54 children are estimated to have ASD, and the recurrence rate—risk of a child having ASD in families who already have one child with autism—is estimated to be 14% (Center for Disease Control, 2016; Zwaigenbaum et al., 2015). Due to the recurrence rate being higher than the general prevalence of autism (1% vs. 14%), children who have an older sibling already diagnosed with autism are considered at "high risk" for autism. A prominent diagnostic characteristic in ASD is a core deficit in social communication. Social communication involves verbal and non-verbal behaviors, such as turn taking in conversations and joint attention that are vital for reciprocal social interactions (Wetherby, Watt, Morgan, & Shumway, 2006). Difficulties with social communication impair one's ability to process social and emotional information and interact with others in social contexts (Sasson, 2006). Associated with social communication impairments are face processing deficits (i.e., difficulties with eye contact, emotion recognition and memory of faces), which are also seen in individuals with autism. The study of face processing deficits in ASD has grown and eye-tracking studies have shown evidence that individuals with autism exhibit abnormalities in their ability to attend to and fixate on people's faces, gazes, expressions and certain features of the face (Frazier et al., 2017). Difficulties attending to faces can be seen as early as 6-months-old in infants who are later diagnosed with autism (Jones & Klin, 2013) and atypical face processing abilities are evident within the first year (Elsabbagh et al., 2012). Due to faces being an essential source of social information, many researchers believe that face processing deficits may be implicated in problems with social functioning in autism (Corbett, Newsom, Key, Qualls, & Edmiston, 2014; Dawson, Webb, & McPartland, 2005; Sasson, 2006).

The Use of Eye-Tracking Methodology

Eye-tracking technology has been widely used to study face processing deficits in autism and has provided researchers with insight into how individuals with autism attend to and process faces. Eye-tracking technology is a non-invasive, video-based method used to record eye movements while individuals view visual stimuli (Karatekin, 2007). Eye-trackers allow researchers to monitor participants' eye movements using corneal reflection, typically from an infra-red light source. In video-based eye-tracking, the eye-tracker estimates the location of the center of the participant's pupil using the corneal reflection of the infra-red light and, subsequently, tracks and measures the participant's gaze behaviors from the movement of the pupils (Duchowski, 2017; Falck-Ytter, Bolte, & Gredeback).

Eye movements and looking behaviors are associated with the ability to attend to and process information, and eye-tracking technology can provide researchers with an objective and quantifiable method to assess these cognitive processes (Duchowski, 2017; Karatekin, 2007). Researchers have examined a wide variety of eye movements and looking behaviors to measure various cognitive processes, such as language, image, auditory, and social processing (Mele & Federici, 2012). For example, an individual's saccades (rapid eye movements between fixation points) are associated with the ability to shift their attention, while the pursuit of an object (smooth movements following a visual target) indicates the ability to visually track an object (Karatekin, 2007). Researchers also commonly examine visual fixations—voluntary eye movements that stabilize over a visual stimulus. Fixations indicate the desire to continually gaze at an object of interest. Therefore, they are typically used as a measure of attention and information processing (Duchowski, 2017). Researchers commonly use Areas of Interest (AOIs) to identify the location and duration of participants' fixations while viewing visual stimuli. For example, when using facial stimuli, researchers commonly mark the eyes, mouth, and whole face as AOIs to determine which parts of the face participants attend to the most. The duration of fixations, typically measured in milliseconds, is used as measure of processing speed (Karatekin, 2007).

Face Processing

Faces provide a multitude of information about an individual's identity, emotions, and non-verbal language cues (Frank, Vul, & Johnson, 2009). Face processing abilities include several skills (i.e., visual scanning, gaze processing, emotion recognition, facial recognition, and facial memory). These skills evolve from the initial ability to attend to and scan faces. Previous research has shown evidence that individuals with ASD exhibit different visual scanning patterns than their typically developing peers. The scope of this meta-analysis aims to investigate when these differences manifest through examination of looking behaviors of infants at high and low risk for ASD.

Typical development of face processing abilities. The ability to process information from faces is vital to learn about our social world. Face processing abilities begin to develop from birth and continue until we achieve an expertise for faces (Frank et al., 2009). Soon after birth, newborns show an interest in faces and prefer face-like stimuli to other non-social stimuli (i.e., a bull's-eye, a colored disk, or a red block) (Fantz, 1963, 1967). Bahrick and colleagues (2016) studied the development of 2-to-8-month-old infants' attention to faces versus objects and found that 3-months-old prefer audiovisual facial stimuli compared to other event types (i.e., audiovisual objects, silent dynamic faces and silent dynamic objects). They also found that their preference for audiovisual facial stimuli was maintained across ages (Bahrick, Todd, Castellanos, & Sorondo, 2016). These findings were consistent with the findings from a previous study by Frank, Vul, and Johnson (2009). Frank et al. examined the gaze patterns of 3-, 6-, and 9-month-old infants viewing a dynamic scene from a children's cartoon. They found that the 3-month-old infants looked at the faces more than other AOIs, such as bodies or hands. However, the 6- and 9-month-old infants looked more at the faces than the 3-month-olds. This indicates that although there is a preference for facial stimuli early in infancy, it becomes more pronounced and consistent throughout development. This increased attention to faces throughout infancy may be due to a rising awareness of faces as a source of social information (Frank et al., 2009).

During the first month of life, infants look more at the outer edges of the face, and it is not until infants are 2-months-old that they begin to broadly scan and fixate on the inner features of the face (Maurer & Salapatek, 1976). By 2- and 3-months-old, infants tend to focus most on the eyes and seldom fixate on the mouth when viewing a face (Hunnius & Geuze, 2004). This preference for the eyes continues through 6 months of age. During this time, eye fixations begin to slightly decrease as infants age, but their fixations towards the mouth do not increase (Lewkowicz & Hansen-Tift, 2011). However, Lewkowicz and Hansen-Tift (2011) found that around 6 to 8 months, there is a shift in infants' attention from the eyes to the mouth. During this period, infants begin to babble and learn language; therefore, watching the speakers' mouth allows them to gain access to audiovisual speech cues which benefit their imitation and understanding of speech. However, they also found that by 12-months-old, infants began to shift their attention away from the mouth back to the eyes. Once infants are exposed to language, their need for audiovisual speech cues decreases. This allows them to begin exploring other social cues that convey non-verbal communication, such as social cues that are relayed through eye contact (Lewkowicz & Hansen, 2011).

Face processing deficits in autism. Children and adults with ASD exhibit irregularities in their face processing abilities, such as reduced eye-to-eye gaze, impaired emotion recognition and diminished memory for faces (Pelphrey et al., 2002; Sasson, 2006). Many researchers believe that these difficulties with face processing tasks contribute to the social communication deficits seen in autism (Pelphrey et al., 2002). In an eye-tracking study conducted by Klin and colleagues (2002), individuals with autism exhibited significantly different gaze behaviors when viewing a dynamic social scene than TD peers. Adolescents and young adults with high-functioning autism watched clips from a movie with complex social scenes, while the researchers measured the participants' fixation time to four AOIs in the scenes: eyes, mouth, body, and objects. They found that individuals in the ASD group fixated 2 times less on the eye region and 2 times more on the mouth region than their TD age-matched peers. Reduced time spent looking at eyes was the greatest predictor of autism (Klin, Jones, Schultz, Volkmar, & Cohen, 2002). Similar to the results of previous studies, Jones, Carr, and Klin (2008) found that 2-year-old children with ASD exhibited less time looking at the eyes than TD children when viewing social stimuli. The participants were shown dynamic videos of a woman speaking and engaging in games like 'pat-a-cake' into the camera as if talking to the child viewing the video. They found that children in the ASD group, compared to age-matched developmentally delayed (DD) and TD children, looked less at the woman's eyes and more at her mouth (Jones et al., 2008). Because of the widespread amount of evidence of abnormal looking behaviors in children with autism has been reported, researchers have begun to investigate sex differences in early social attention within autism. Previous research has found that boys and girls with autism exhibit different looking patterns. Boys at high familial risk for autism were found to look more at the mouth than high risk girls (Kleberg, Nystrom, Bolte, & Falck-Ytter, 2018). Chawarska and colleagues (2016) also found that girls at high risk for autism looked longer at the face when viewing a video of a woman speaking than high risk boys or low risk controls. Studies testing face processing abilities have also shown that when an emotional component is included in the task, performance is worse and evidence of impairments are greater in individuals with autism (Wang et al, 2004). Research has shown that when looking at emotional faces, children and adolescents with autism have diminished gaze fixation towards the eyes when looking at faces exhibiting negative emotions, such as anger and fear (Davies, Bishop, Manstead, & Tantum, 2011). Reduced eye contact has many implications in the development of face processing abilities and social communication. The ability to recognize and interpret gaze cues and orient attention to where others are looking (i.e., joint attention) is important for effective social communication (Wang, Dapretto, Ahmad, Sigman, & Bookheimer, 2004). Previous research has indicated that time spent looking at the eyes is negatively correlated with social competence, implying that decreased eye fixations in individuals with ASD are associated with greater levels of social impairment on the Autism Diagnostic Observation Schedule (ADOS) (Jones et al., 2008; Tang et al., 2017). More time spent fixating on mouths and objects has also been associated with decreased social functioning (Klin et al., 2002). These findings indicate that abnormal visual fixation patterns compared to those of typically developing individuals can predict social deficits in ASD.

While eye-tracking research has shown evidence that individuals with autism exhibit unique scanning patterns when viewing faces, studies have also shown that children with autism orient and attend less to socially relevant information, in general, than their TD peers (Guillion, Hadjikhani, Baduel, & Roge, 2013). Shic and colleagues found that 20-month-old toddlers with ASD looked less at the people in a social scene when viewing a video of an adult-child interaction than both toddlers with non-autistic DD and TD toddlers; the ASD group focused more on the background objects. Furthermore, when the participants in the ASD group did attend to the people, they spent significantly less time looking at their faces and more time looking at their bodies (Shic, Bradshaw, Klin, Scassellati, & Chawarska, 2011). Researchers report similar findings when examining the fixation patterns of 1- and 3-year-old children with ASD compared to their TD peers. The participants watched a video of two women engaging in a conversation. The children with ASD spent less time looking at the women's faces than the TD children at both 1- and 3-years-old (von Hofsten, Uhlig, Adell, & Kochukhova, 2008). These differences in looking behaviors may indicate that children with ASD are not as interested in social stimuli as TD children and, therefore, attend less to social information.

The importance of the stimulus. Although there are many studies that support the claim that children with autism look less at the eyes and more at the mouth when compared to typically developing children, there are also studies that show no significant differences in facial scanning between the two groups. These discrepancies in the literature may be due to the use of different types of stimuli (Chawarska & Shic, 2009). Eye-tracking studies have provided evidence that when individuals with ASD watch dynamic stimuli, they spend more time looking at the mouth, but when they view static images of faces, they have similar fixation patterns to TD children (Klin et al., 2012). The variability of eye-tracking study results led Chevallier and his associates (2015) to conduct a study examining how different types of social stimuli affect looking behaviors and social attention—attention to socially relevant information—in individuals with ASD. They hypothesized that more ecological, dynamic stimuli would better depict how children behave in real-world situations and yield the greatest differences in social attention and gaze behavior between the ASD group and TD controls. Children and adolescents aged 6-17-years-old were shown static images of objects and faces ("Static Visual Exploration"), silent dynamic video clips of objects and faces ("Dynamic Visual Exploration") and silent interactive video clips of children playing with objects on a table ("Interactive Visual Exploration"). In the "Interactive Visual Exploration" task, the ASD group spent less time looking at the social stimuli (pairs of school-aged children playing with objects) than the TD group. However, because of the difference in sizes of AOIs between the tasks, researchers were unable to make within-group comparisons for stimulus type. For example, because object AOIs are larger in the "Static Visual" and "Dynamic Visual" conditions than the "Interactive Visual" condition, it is difficult to compare fixation times. The researchers could not determine if fewer fixations on the objects in the "Interactive Visual" condition were due to the task or the size of the AOIs. Additionally, the researchers did not compare the amount of time children in the ASD group fixated on the social stimuli across conditions. It would have been beneficial to determine if children and adolescents with ASD looked less at the children playing in the "Interactive Visual" condition than the faces in the "Dynamic Visual" clips and "Static Visual" images in order to more definitively determine if children with ASD fixate less on people when viewing dynamic stimuli. Alternatively, we can still conclude that the greatest differences in gaze patterns between the autism group and typically developing group were seen in the interactive task, when the task represented the most naturalistic and ecologically valid depiction of social stimuli. This indicates that individuals with ASD may exhibit reduced attention to social actions as opposed to just social beings. Although static images of faces are social stimuli, they likely do not provide as much social information or depict real-world social behaviors and, subsequently, are less influential in eliciting social responses (Chevallier et al, 2015).

Chawarska and Shic (2009) further supported the impact of stimulus type when they examined the face scanning patterns of 2- and 4-year-old children with autism. When presented with a static color image of a neutral female face, both the 2- and 4-year-old ASD groups spent more time looking at the eyes than any other part of the face. When viewing still images, more looking at the eyes might indicate that the eyes are more perceptually salient because of the contrast of the sclera and iris, and that children with autism may be driven by a "heightened sensitivity to low-level perceptual features," (Chawarska & Shic, 2009). Interestingly, the 2- and 4-year-old ASD groups also spent less time looking at the mouth than the TD age-matched groups. Therefore, the mouth may not be as salient of a feature as the eyes for the ASD group, and because of the lack of speech, there is not a desire to look at the mouth in order to achieve audiovisual synchrony (Chawarska & Shic, 2009). These findings suggest that reduced eye contact might only be evident when the eyes convey social cues, semantic information, and truly act as a source of social communication, which is not evident in static photos (Chawarska & Shic, 2009; Davies et al., 2011). Therefore, based upon a review of these studies, the primary findings show that individuals with autism may only exhibit reduced eye fixations and increased looking at the mouth when viewing dynamic stimuli.

Theories of Face Processing Deficits in Autism

Researchers have debated the underlying causes of face processing deficits in autism. Three of the leading hypotheses are the perceptual, gaze aversion, and social motivation hypotheses.

Perceptual hypothesis. The perceptual hypothesis argues that individuals with autism have a preferential bias for local processing and exhibit a more featural processing style as opposed to the configural processing style seen in typically developing children. This theory explains that individuals with autism have difficulties processing faces because they look at the features of the face, but fail to see the face as a whole, and this scanning pattern later disrupts their ability to recognize and discriminate between faces (Behrmann et al, 2006). Behrmann and colleagues (2006) examined the role of the perceptual hypothesis in face processing abilities in adults with autism. Participants were shown pairs of grey-scale faces side by side on a computer and were asked to identify whether the two faces were different genders or different individuals. The "individual" discrimination task required a greater level of global processing, and the results showed that the autism group had significantly slower reaction times when discriminating between individuals versus gender. When the task required individuals with ASD to employ global processing strategies, they exhibited slower processing speed than their TD peers (Behrmann et al, 2006). Morin and colleagues (2015) also tested this hypothesis by examining adolescents (13-17 years) and adults (18+ years) with autism on face perception tasks that required local and global processing. The participants performed a facial identity discrimination task that presented faces in the same direction and at a viewpoint change. The faces in the same direction allowed the participants to view features of the face, but the viewpoint change condition required global analysis of the face as a whole (Morin et al, 2015). Results of the study showed that the autism group performed worse than the control group on the discriminatory task when in the viewpoint change condition, even though they did comparable to the typically developing group on all other conditions. Their worsened performance in attributed was attributed to their inability to access global information from faces (Morin et al, 2015).

Gaze aversion hypothesis. The second hypothesis, gaze aversion, states that individuals with autism become over-aroused when looking at the eyes and develop an aversion for mutual gaze. This aversion to eyes results in failure to acquire expertise for faces and develop efficient face processing abilities (Davies, Dapretto, Sigman, Sepeta & Bookheimer, 2011). The gaze aversion hypothesis has been linked to increased activation in the amygdala, the brain region involved in processing negative emotional expressions such as anger and fear. Dalton et al. (2005) conducted a study to examine the relationship between eye gaze and brain activation in emotionally-responsive brain areas. They predicted that individuals with autism would show hyper-activation in the amygdala and said amygdala activation would be dependent on time fixating on the eyes (Dalton et al., 2005). Adolescents, approximately 15-years-old, participated in a facial emotion discrimination task, during which participants looked at faces displaying emotional expressions while researchers acquired their functional magnetic resonance imaging (fMRI) data and eye movements. Consistent with the researchers' predictions, the results showed that the ASD group exhibited significantly greater activation than the control group in the amygdala and orbitofrontal gyrus, areas associated with emotion processing. To further support the gaze aversion hypothesis, they calculated a correlation between participants' time spent fixating on the eye and their amygdala activation. Eye fixations in the emotion discrimination task strongly and positively predicted amygdala activation in the autism group, but not the control group. These results indicated that not only do individuals with autism have heightened sensitivity to emotional cues, but also that eye fixation is associated with hyper-activation in the amygdala (Davies et al., 2011). According to the gaze aversion hypothesis model, individuals with ASD are overstimulated when looking at the eyes, and reduced gaze fixations may alleviate these arousal-provoking responses to the eyes. This, in turn, results in diminished exposure to the eyes and a decline in expertise and overall face processing abilities.

Social motivation hypothesis. The social motivation hypothesis states that individuals with autism lack the desire to attend to faces because they do not find them intrinsically interesting or salient, which causes diminished experiences and expertise for faces and eventually hinders the development of social cognition (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012; Dawson et al, 2005). This theory hypothesizes that social information is less rewarding for individuals with ASD than typically developing individuals, which lowers their motivation to seek out social stimuli (Chevallier et al., 2012). This evidence of decreased eye fixations is consistent with the hypothesis that a lack of interest in social stimuli in individuals with autism results in diminished motivation to attend to faces and look at eyes (Dawson et al., 2005). Lack of social motivation has also been attributed to abnormalities in reward systems and neural systems involved in perception of social rewards, such as the dopamine system and orbitofrontal-striatum-amygdala network (Chevallier et al., 2012). Children with ASD exhibit reduced neural responses in these areas when viewing facial stimuli compared to TD peers (Scott-Van Zeeland, Dapretto, Ghahremani, Poldrack, & Bookheimer, 2010). As a consequence, reduced interest in social information results in difficulties with the development of social cognition skills, such as joint attention (Chevallier et al, 2012).

The First Year

On average, children with autism are diagnosed around 3-years-old. By that time, there are clear impairments in social and nonsocial domains of functioning, and face processing abilities are significantly diminished compared to TD children (Elsabbagh et al., 2011). However, once diagnosed, children with autism can learn strategies to compensate for their difficulties in social communication and exhibit behavioral performance within the typical range (Elsabbagh et al., 2011). With intervention, less than 10% of children with low functioning autism who are non-verbal will remain non-verbal; additionally, children who receive these interventions in the early pre-school years are more likely to become verbal than children who begin after the age of 5 (Koegel, 2000). Research has shown that when children with autism receive early intervention, there are significant gains in cognitive, social, and adaptive skills (Dawson et al., 2010). Dawson and colleagues (2010) found that when children between 18 and 30 months (1.5-2.5 years) with ASD received early intervention using the Early Denver Start Model—a comprehensive behavioral intervention program for children diagnosed with autism—they exhibited significant gains on the cognitive, language, and adaptive behaviors compared to children with ASD who received community intervention. Taken together, these findings highlight the importance of early identification and treatment of autism symptomatology. Many researchers have started examining the emergence of autism symptoms in infants at high risk for autism in hopes to discover ASD markers earlier (Elsabbagh et al., 2011). A retrospective study found that a failure to look at others during their first birthday was an evident behavioral marker for infants who were later diagnosed with autism (Osterling & Dawson, 1994). Inattention to faces and delayed face-related social milestones are evident at as early as 1-year-old (Dalton et al., 2011), and differences in time fixating on eyes in social scenes can be seen as young as 6-months-old (Jones & Klin, 2013); therefore, face processing deficits may be one of the earliest signs of autism symptoms (Dawson et al., 2005).

The Current Study

Abnormal visual scanning of faces in individuals with autism is a predictor and possible precursor to more prominent social communication deficits seen in autism (Klin et al., 2002;

Sasson, 2006) and it is one of the earliest symptoms (Dawson et al., 2005). There is a great deal of research regarding face processing deficits, however, there are inconsistencies in the findings due to variability in symptomatology across ages and the types of stimuli used in eye-tracking studies. Additionally, there is still very little known about when these face processing deficits begin to emerge and when the differences in abilities between children with autism and TD children become clear. Furthermore, no meta-analyses have been conducted on the emergence of face processing deficits in infants at risk for autism or on the effect of stimulus type on viewing social stimuli when using infant participants.

The aim of the present meta-analysis is to determine the degree and significance of differences in looking behaviors between infants at high and low risk of autism, and to examine if these differences are affected by the type of social stimuli used. We aim to compare infants at high and low risks' looking behaviors when viewing static stimuli, dynamic stimuli, and when participating in the still-face paradigm. The still-face paradigm consists of three episodes: the Face-to-Face episode, the Still-Face episode, and the Reunion. Caregivers were asked to play with their infant without toys for three minutes, stop playing and hold a still-face for a minute or two, and then resume play. Studies using the still-face paradigm were include in this meta-analysis due to the use of naturalistic interactions. We consider the still-face paradigm to be a better representation of infants' real-world social behaviors than static and dynamic stimuli and therefore, would elicit more accurate social responses in both groups. By synthesizing the available infant studies data in autism research, we hope to provide clarity on the trajectory, patterns, and factors associated with face processing deficits seen in autism.

The following research questions were examined in this meta-analysis:

1. What is the magnitude of differences in looking behaviors in infants at high and low risk when they view social stimuli?
2. Are the differences in looking behaviors greater when participants are viewing dynamic stimuli, static stimuli, or when participating in the still-face paradigm?
3. Are differences in looking behaviors between high and low risk infants greater as they increase in age?

CHAPTER II: METHODS

The Selection Process

The East Carolina University (ECU) online library database was used to systematically search for studies to include in this meta-analysis. ECU's online libraries have access to over 100 databases, including PsycINFO, SAGE Research Methods, and the Wiley Online Library. The following search terms were used to search for articles pertaining to the use of eye-tracking to examine face processing abilities in infants at risk for autism: ("infants at risk" AND "autism" AND "eye-tracking" AND "social attention" AND "faces"). With the advanced search options, we limited the search to only include articles that were published in English.

The literature search produced 4,527 results. Studies were not limited by date; however, the literature search was concluded on June 10th, 2018; thus, all studies were published before June 2018. Items were excluded if they were Books or Newspaper Articles. The rest of our search only included Journal Articles, Publications and Theses/Dissertations, which equated to 1,116 studies. The titles and abstracts of these 1,116 articles were examined, and 924 studies were removed for lack of relevance (i.e., use of children instead of infants or only typically developing infants). The remaining 192 studies were thoroughly reviewed and entered into an excel file, marking Yes or No for meeting the following criteria:

1. The article included an empirical study and was not a review, meta-analysis or critique
2. The study utilized infants (birth to 12 months) both at high risk and low risk for developing autism. Infants at high risk for autism are defined as an infant that has an older sibling with a confirmed diagnosis of autism spectrum disorder.

3. The study used an eye-tracker and measured duration of time looking at or time fixating on the stimulus.
4. The study used facial stimuli, such as a dynamic video of a person, photographs of a face, or the still-face paradigm. Studies were excluded if the stimulus was a retrospective home video or only included shapes or objects.
5. The study included effect sizes or data that could be used to calculate an effect size.

These criteria were selected to identify studies that examined the differences between infants at high risk and low risk's looking behaviors when viewing social stimuli. Each study was initially coded by the first author and coding was then checked by undergraduate research assistants trained in the coding procedure. In total, 21 articles met all of the criteria and were included in the meta-analysis. Nineteen of the included articles were published studies, while 2 were Master's theses. Other than irrelevance, the most common reasons studies were excluded was because they did not use an eye-tracker or facial stimuli (Figure 1).

Publication Bias

The "file drawer" problem refers to the possibility that meta-analyses using only studies included in peer-reviewed journals are not representative of all of the studies conducted because studies that fail to find significant results are hidden away in researchers' file drawers. This problem occurs because studies finding null or negative results are less likely to be published—publication bias (Card, 2012). Due to published studies typically having significant results, meta-analyses that exclusively include published studies may yield an estimated mean effect size that is considerably higher than in the true population of the studies conducted.

To manage the possible publication bias within this meta-analysis, a call for unpublished studies was emailed to two listervs, in which we believed our research would be relevant:

Intellectual and Developmental Disabilities/Autism Spectrum Disorder and the Cognitive Development Society. However, we did not receive any studies from the listervs. Additionally, a funnel plot (Figure 3) and rank-sign correlation between sample size and effect size were generated. A funnel plot is a scatterplot of all of the effect sizes of the studies included in the meta-analysis, and it is used to evaluate publication bias (Card, 2012). In a funnel plot, it is expected that studies with small sample sizes will have a larger variability in effect sizes; however, as sample sizes increase, the variability in effect sizes should decrease, due to smaller standard errors. A regression test of funnel plot asymmetry was used to assess the symmetric distribution of points within the funnel plot. If the funnel plot is symmetric, we can assume the dataset is well-balanced and does not display a publication bias. To further test publication bias, we used the Begg-Mazumdar rank correlation test to assess the interdependence of studies' sample size and effect size.

Data Analysis

Meta-analyses were conducted using the *metafor* package (Viechtbauer, 2010) in R (R Core Team, 2020). All analyses were conducted using random effects models, due to the studies' differing sampling and methodological factors. For studies examining differences in visual scanning of eyes versus mouth when viewing facial stimuli, an Eye-Mouth Index (EMI) was calculated. EMI is a percentage or duration of gaze time to the eyes out of the total time infants attended to either the eyes or the mouth (Eyes/(Eyes + Mouth). An EMI less than 0.50 indicates that infants looked relatively more at the mouth; a high EMI, above 0.50, indicates that infants looked relatively more at the eyes (Merin, Young, Ozonoff, & Rogers, 2006). Many studies also examined infants' duration of fixations towards social stimuli (faces) and non-social stimuli (body parts, background scenes, objects, etc.) To further examine patterns of looking towards social versus nonsocial stimuli for infants at risk, we calculated a Social-Nonsocial Index (SNI). SNI is the percentage or duration of gaze time to a face out of the total time infants attended to either the face or the other stimuli within the scene (Social/Social + Nonsocial). An SNI less than 0.50 indicates infants looked more at the nonsocial stimuli within the scene, while an SNI greater than 0.50 means infants looked more at faces than the other stimuli. Lastly, some studies examined high and low risk infants' general proportion of looking towards faces during the eye-tracking task.

The extent of differences in looking behaviors for infants at high and low risk for autism was assessed using Cohen's *d.* Cohen's *d* was calculated as the effect size measure—the difference between the means of two groups divided by the pooled standard deviations—for each of the three outcome measures. A positive Cohen's *d* indicated that infants at high risk for autism exhibited higher EMI, SNI or proportion of looking to faces compared to the control group. The effect size was interpreted according to Cohen's classification of effect sizes: small = 0.2, medium = 0.5, and large = 0.8 (Cohen, 1988).

CHAPTER III: RESULTS

Twenty-one studies published from 2006 to 2018, which tested 1990 infants at high (n = 1090) and low risk (n = 900) for autism, met our criteria. A total of 25 comparisons were conducted to assess the overall differences in visual scanning patterns in infants at differing risks for autism. There were some overlaps in participant groups, as four studies examined multiple outcomes variables (i.e., EMI and SNI). Therefore, three separate meta-analyses were conducted to examine the pattern of effects for each outcome variable. Thirteen comparisons assessed participants' Eye-Mouth Index (EMI), 9 measured fixations to social vs. non-social stimuli (SNI), and 3 examined proportion of fixations towards the face as the outcome variable. Sixteen comparisons used static photographs of faces, 5 used dynamic stimuli, and 4 used the still-face paradigm as their visual stimuli. Sample sizes ranged from 34 to 162 participants, and the mean age of participants ranged from 4.99 to 11 months old. A regression test of funnel plot asymmetry failed to find significant evidence of publication bias ($z = -1.11$, $p = 0.267$); however, the Begg-Mazumdar rank correlation test indicated a significant relationship between studies' sample size and effect size ($\tau = -0.42$, $p = 0.007$), implying possible publication bias.

General Visual Scanning Patterns

For the primary analysis, we included 21 comparisons, combining all three outcome variables, that examined the overall visual scanning patterns observed during eye-tracking tasks. For the four studies that utilized the same participants to assess multiple outcome measures, we averaged the effects of each study to form one study effect size. From a random effects analysis of overall effect size, we found a mean effect size of $d = 0.04$ ($\tau^2 = 0$) with 95% confidence interval limits from -0.06 to 0.14 (Figure 2). A positive effect size indicates greater looking towards social stimuli in infants at high risk for autism than controls; however, this is a small effect size and does not yield a statistically significant difference between groups, $p = 0.406$.

Moderators. We considered the impact of three moderator variables on visual scanning patterns- the average age of participants, percent of male infants in the autism group, and the type of visual stimuli used. Three separate analyses were conducted to assess the individual effect of the three moderators on the full model. There were no significant effects of average age ($b = 0.03$, $p = 0.328$), percentage of male participants ($b = -0.01$, $p = 0.278$), or type of stimuli ($Q= 2.69$, $p = 0.261$). These results indicate that the average age of the participants and the number of male participants did not have a significant impact on the difference, or lack thereof, in looking behaviors between infants at high and low risk for autism. Additionally, when comparing studies with different types of stimuli, there was not a significant difference in the average effect sizes (Figure 4).

Visual scanning and stimulus type. To further assess the effects of stimulus type on infants' looking behaviors, we conducted three separate meta-analyses to analyze the average effect sizes when using each type of visual stimuli. When comparing studies that used static stimuli (images of faces), we found that infants at high and low risk did not differ in their looking behaviors ($d = 0.02$, 95% CI -0.10 – 0.13, $p = 0.756$, $\tau = 0$). The comparisons for studies using dynamic stimuli (videos of faces and scenes) also showed that infants did not differ in their visual scanning patterns between groups ($d = 0.12$, 95% CI -0.05 – 0.30, $p = 0.166$, $\tau = 0$). Lastly, we examined the effect of differences in looking behaviors when using the still-face paradigm, the most ecological of the three types of social stimuli. We found that infants at high and low risk did not differ on looking behaviors towards a parent's face when interacting in the still-face paradigm ($d = -0.15$, 95% CI -0.46 – 0.15, $p = 0.324$, $\tau = 0.10$).

Visual Scanning Patterns by Outcome

We further assessed infants visual scanning behaviors using three outcome variables: EMI, SNI and proportion of fixations to faces. Twelve studies, involving 13 comparisons, assessed differences in EMIs in infants at risk for autism compared to controls. Overall, there was not a significant difference between groups in percentage of looking at the eyes versus the mouth (d = 0.03, 95% CI -0.10 – 0.16, p = 0.660, τ = 0). The high risk group had an average EMI of 0.72 (SD = 0.23), and the low risk group's average EMI was 0.68 (SD = 0.24). Overall, both the high and low risk groups looked more at the eyes than the mouth when viewing a face. We assessed the moderators of age, gender and stimuli on the EMI effect size. Neither age (b = 0.02, p = 0.63), gender (b = 0.32, p = 0.623), nor stimuli (b = 0.01, p = 0.958) moderated the relationship of risk status on EMI.

Nine studies (9 comparisons) were used to examine the percent of time that infants at differing levels of risk for autism viewed social stimuli versus nonsocial stimuli. Our meta-analysis revealed there was not a significant difference in looking behaviors for high risk compared to low risk infants (d = 0.01, 95% CI -0.14 – 0.16, p = 0.889, τ = 0). The high risk group (M = 0.74, SD = 0.49) and the low risk controls (M = 0.72, SD = 0.43) both looked more at the social stimuli (faces) than the nonsocial stimuli (i.e., objects and background scenes) as opposed to looking at each type of stimuli equally. The moderating effects of age (b = 0.02, p = 0.415), gender (b = -0.01, p = 0.318), and stimuli (b = -0.03, p = 0.773) were non-significant.

Three studies assessed the infants' visual fixations towards the face but did not calculate the duration of fixations towards non-social stimuli. Due to the inability to compute the looking behaviors into a ratio as we did for SNI, we conducted a separate meta-analysis, with three comparisons, to assess the proportion at which infants at varying risk fixated on faces. The analysis showed there was not a significant difference between the two groups (d = 0.09, 95% -0.17 – 0.36, p = 0.493, $\tau = 0$). When looking at a general scene, infants at high and low risk viewed faces for similar proportions of time. Due to the distributions of sampling variances, moderator analyses could not be conducted for age, gender, and type of stimuli.

CHAPTER IV: DISCUSSION

The current study aimed to assess the difference in how infants at high and low risk visually scan socially salient stimuli within the first year of life. Reduced eye contact and decreased orienting to faces have been noted as important markers for identification of ASD at 12 months and persist throughout the second year of life (Barbaro & Dissanayake, 2012; Osterling & Dawson, 1994). Appropriate eye contact is currently used as a behavioral marker to help identify ASD in children. Currently, the presence of eye contact is used as one of the criteria to help assess and diagnosis autism on the Autism Observation Diagnostic Schedule, Second Edition (ADOS-2) and is an item on the Modified Checklist for Autism in Toddlers (MCHAT) screening tool. Reduced eye contact is thought to begin by 12-months-old and effects children across the entire spectrum. On the Autism Observation Scale for Infants (AOSI)—a measure aimed at assessing behavioral manifestations of autism in the first year of life—atypical eye contact and social interest at 12-months predict autism at 24-months (Zwaigenbaum et al., 2005). However, the studies within our meta-analysis revealed varying results regarding the visual scanning patterns of infants at risk for ASD.

Multiple meta-analyses were conducted to measure the effect of infant risk status on three outcome looking behaviors: EMI, SNI, and proportion of time looking to faces. On average, the combined looking behavior patterns of infants at high risk for autism were similar to those of low risk infants. All but one of the studies' confidence intervals included zero, indicating the effect sizes of the studies were not statistically significant. However, 10 comparisons found at least a small effect in the difference in looking behaviors between infants at high and low risk. Surprisingly, six comparisons found that infants at high risk looked more at the social stimuli, while the other four found the opposite effect. The inconsistency of the combined results of the studies yielded an overall nonsignificant effect size of approximately zero. When assessing the individual outcome measures, the meta-analytic results showed that high risk and low risk infants exhibited similar EMI, SNI and proportions of looking towards faces. Infants at high risk looked at the eyes versus the mouth at similar rates to infants at low risk for autism. Additionally, infants at high risk exhibited similar looking behaviors to infants at low risk when viewing social scenes. Both groups looked more at faces than features of the scene.

Meta-regression analyses were conducted to determine how different factors, such as age, gender, and stimulus type, may moderate the looking behaviors seen in infants at risk. The results indicated that, overall, our sample of studies did not show a significant difference in how infants at varying risks look at social stimuli regardless of age, gender, and stimulus type. When looking at static and dynamic stimuli, infants at high and low risk both looked more to the eyes than the mouth and more to faces than other non-social stimuli at similar ratios. During the still-face paradigm, infants at high risk looked to their caregivers' faces at comparable rates to infants at low risk for autism. Overall, we found that infants at high risk do not significantly differ in visual scanning patterns when viewing faces compared to infants at low risk, regardless of age, gender, or stimulus type.

Limitations

Although a comprehensive sample of studies were reviewed, we were not able to use several studies that were deemed eligible to be included in the meta-analysis due to lack of access to data or an inability to compute effect sizes for our comparisons. Eight studies did not include the appropriate effect sizes. We reached out to the study authors for their raw data; however, only two authors responded. Thus, some data was lost, decreasing our sample size and statistical power. Furthermore, majority of the studies (66.67%) used static stimuli, with which previous studies had not shown many differences between low and high risk infants (Chevallier et al., 2015; Klin et al., 2012). Also, only 3 of 21 studies (14.28%) used the still-face paradigm, which we considered the most socially ecological form of stimuli and expected to yield the greatest differences in looking behaviors between groups. Additionally, some studies examined the effect of looking behaviors based on their diagnostic outcome later in childhood. For example, many studies grouped their participants as low risk, typically developing high risk, or atypically developing high risk infants. In order to compare groups by risk status, we compiled outcome group data into risk groups. With this process, some of the effect differences between groups may have been lost. High risk infants who were found to have autism later in childhood may have exhibited statistically different looking behaviors than typically developing low risk infants. However, compiling the groups by risk status may have caused results to regress towards the mean. Furthermore, some studies examined infants' patterns of looking behaviors towards faces in different emotional conditions. Emotional face processing was outside of the scope of this meta-analysis; therefore, we compiled the data from each emotion condition together to obtain average looking durations for each risk group. As with the comparison groups, compiling the data from each emotional condition may have diluted the differences in looking behaviors for high and low risk infants. Previous research has found that individuals with ASD look less at the eyes than the mouth when viewing faces with negative facial expressions. Therefore, we may have found greater effects between groups if differences in looking behaviors during emotion conditions were examined separately. Additionally, many studies examined eye-tracking behaviors as a secondary outcome. Face recognition, gaze direction, pupil dilation, and ERP acquisition are some examples of primary outcome measures assessed in the studies with eye-tracking as a secondary measure. Lastly, the typical pattern of looking behaviors towards the eyes and the mouth vary across the first year of life. For example, 2-3-month-old and 6-month-old infants tend to look more at the eyes, while 6-8-month-old infants look more at the mouth. Due to our limited amount of studies, with so few having participants of the same age, it is difficult to get a clear picture of how age moderates looking behaviors in infants at risk for autism. Additionally, our analyses had low statistical power due to our small sample sizes, especially for moderators. Future research using longitudinal studies with large sample sizes is needed to examine the development of looking behaviors in infants at high risk for autism compared to typically developing infants. Future research should aim to address these limitations to gain a further understanding of the development of face processing deficits in infants at risk for autism.

Implications

These findings may have important implications for early identification and diagnosis of autism and clinical practices. Reduced eye contact may not be as reliable of a behavioral marker within the first year of life as previous research has indicated. Poor eye contact and decreased orienting to faces may not yet be consistently apparent within the first year of life; therefore, appropriate eye contact may not act as a reliable universal screener to assess the presence of early autism symptoms. Some infants later diagnosed with autism may fail to show any early signs of social communicative deficits and exhibit typical looking behaviors. It is possible that reduced looking to eyes is only present in infants with the highest level of autism symptoms this early in life. Sixteen percent of the studies included in our analysis found a small to medium effect that infants at high risk for autism looked less at social stimuli than infants at low risk. Although they made up the least amount of data within the meta-analyses, the studies using the still-face paradigm exhibited the greatest effect sizes and were most consistent with previous literature on the looking patterns of children diagnosed with autism. Three out of four comparisons found that infants at high risk looked less at social stimuli than non-social stimuli. These results may indicate that differences seen between infants at high and low risk are most evident and consistent when the stimuli are especially ecological and has high social demands. Some studies (Shic, Macari, & Chawarska, 2014; Hannigen, 2014; Wass et al., 2015) also found that when grouped by diagnostic outcome at 24 months, infants who were later diagnosed with ASD looked less at the social stimuli than their typically developing peers. Infants who exhibit abnormal looking behaviors so early in life may exhibit more severe autism symptomatology later on. However, it is possible reduced eye contact is not a universal indicator of the presence of autism. Due to the inconsistency of atypical looking behaviors, typical eye contact may not rule out a child as having autism. While previous research has suggested that as many as 40% of high risk infants present with marked symptoms within the first year of life (Macari et al., 2012), this also indicates many children may not manifest symptoms until the second year of life, after a period of typical development (Ozonoff et al., 2008). At their first birthday, some children with autism may pass their early ASD screenings; therefore, it is important to repeat screenings to capture children who do not exhibit autism symptoms as early on.

Conclusion

The aim of this meta-analysis was to examine how infants at high familial risk for autism viewed features of faces and faces within a scene compared to low risk infants. Taken together, our findings showed both high and low risk infants exhibit similar looking patterns within the first year of life, regardless of their gender, age or type of visual stimuli. These findings indicate that the development of face processing deficits later seen in children with autism are heterogeneous and may not manifest for some until the second year of life. However, the most consistent results are seen when the stimuli are naturalistic and socially salient. Additionally, many of the studies found significant differences between high and low risk infants when using emotional stimuli, which displays more social information. Studies also found significant differences in looking behaviors when comparing infants by their outcome groups at 24 months. While the findings of this meta-analysis do extend our knowledge of autism symptomatology in infants at risk for autism, an analysis of looking behaviors of children 12-24 months-old and research using physiological and neuroimaging methods would be beneficial. Future studies should also focus on infants' looking behaviors when viewing faces in person (i.e., still-face paradigm or naturalistic parent-child interactions) or when viewing socially salient stimuli with high social demands (i.e., emotional dynamic stimuli).

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Table 1.

Meta-Analysis Study Characteristics

Authors	Mean age (Months)	HR N (% Male)	LR N (% Male)	Stimuli Type	Outcome Measure	Effect Size (Variance)
Chawarska, Macari, Powell, DiNicola, & Shic (2016)	9	101 (70%)	61 (52%)	Dynamic	SNI	**0.02** (0.3)
de Klerk, Gliga, Charman, & Johnson (2013)	7.84	44 (43%)	40 (30%)	Static	SNI	**0.26** (0.05)
Dundas, Gastgeb, & Strauss (2012)	9.06	22 (39.64%)	16 (44.95%)	Static	EMI	**-0.12** (0.12)
Elsabbagh et al. (2012)	7.35	40 (38.89%)	45 (58%)	Dynamic	EMI	**0.19** (0.04)
Elsabbagh et al. (2012)	7.83	54 (38.89%)	50 (42%)	Static	Proportion of faces	**0.13** (0.05)
Elsabbagh et al. (2014)	7.35	54 (38.89%)	50 (50%)	Dynamic	EMI	**0.06** (0.04)
Hannigen (2014)	9.08	34 (57%)	30 (53.5%)	Static	EMI	**-0.02** (0.06)
Hannigen (2014)	9.08	34 (57%)	30 (53.5%)	Static	Proportion of faces	**0.02** (0.06)
Hendry et al. (2018)	9.03	94 (57.45%)	23 (56.52%)	Static	SNI	**0.02** (0.05)
Ibanez (2008)	6.12	17 (58.8%)	17 (47.1%)	Still-Face Paradigm	SNI	**-0.33** (0.12)

Key and Stone (2012)	9.11	20 (60%)	15 (65%)	Static	EMI	**-0.05** (0.12)
Klegberg, Nystrom, Bolte, & Rogers (2007)	10.20	70 (48%)	29 (41%)	Static	EMI	**0.03** (0.04)
Merin, Young, Ozonoff, & Rogers (2007)	5.99	31 (48.38%)	24 (66.67%)	Still-Face Paradigm	SNI	**0.20** (0.07)
Merin, Young, Ozonoff, & Rogers (2007)	5.99	31 (48.38%)	24 (66.67%)	Still-Face Paradigm	EMI	**-0.44** (0.08)
Rutherford (2013)	4.5	31 (58.07%)	61 (57.38%)	Static	EMI	**-0.27** (0.05)
Rutherford (2013)	4.5	31 (58.07%)	61 (57.38%)	Static	SNI	**-0.38** (0.05)
Rutherford, Walsh, & Lee (2015)	7.5	21 (52.38%)	31 (48.39%)	Static	EMI	**0.29** (0.08)
Shic, Macari, & Chawarska (2014)	6.37	57 (67%)	42 (79%)	Static	EMI	**-0.02** (0.04)
Shic, Macari, & Chawarska (2014)	6.37	57 (67%)	42 (79%)	Dynamic	EMI	**0.44** (0.04)
Sperle (2018)	11	47 (63.83%)	39 (51.28%)	Static	SNI	**0.18** (0.05)
Tsang, Johnson, Jeste, & Dapretto (2019)	7.63	34	23	Dynamic	Proportion of faces	**-0.01** (0.08)
Wagner, Luyster, Tager-Flusberg, & Nelson (2016)	9.24	29 (55%)	20 (58.6%)	Static	EMI	**-0.03** (0.09)

Wagner, Luyster, Moustapha, Tager-Flusberg, & Nelson (2018)	7.61	37 (56.75%)	40 (57.6%)	Static	EMI	**0.06** (0.05)
Wass et al. (2016)	6.36	45 (35.56%)	49 (40.82%)	Static	SNI	**0.00** (0.04)
Yimiya, Gamiel, Pilowsku, Feldman, Baren-Cohen, & Sigman (2006)	4.99	21 (61.9%)	21 (85.7%)	Still-Face Paradigm	SNI	**-0.12** (0.10)

Figures

Figure 1. Literature search flow diagram modeled after the PRISMA guidelines flow diagram.

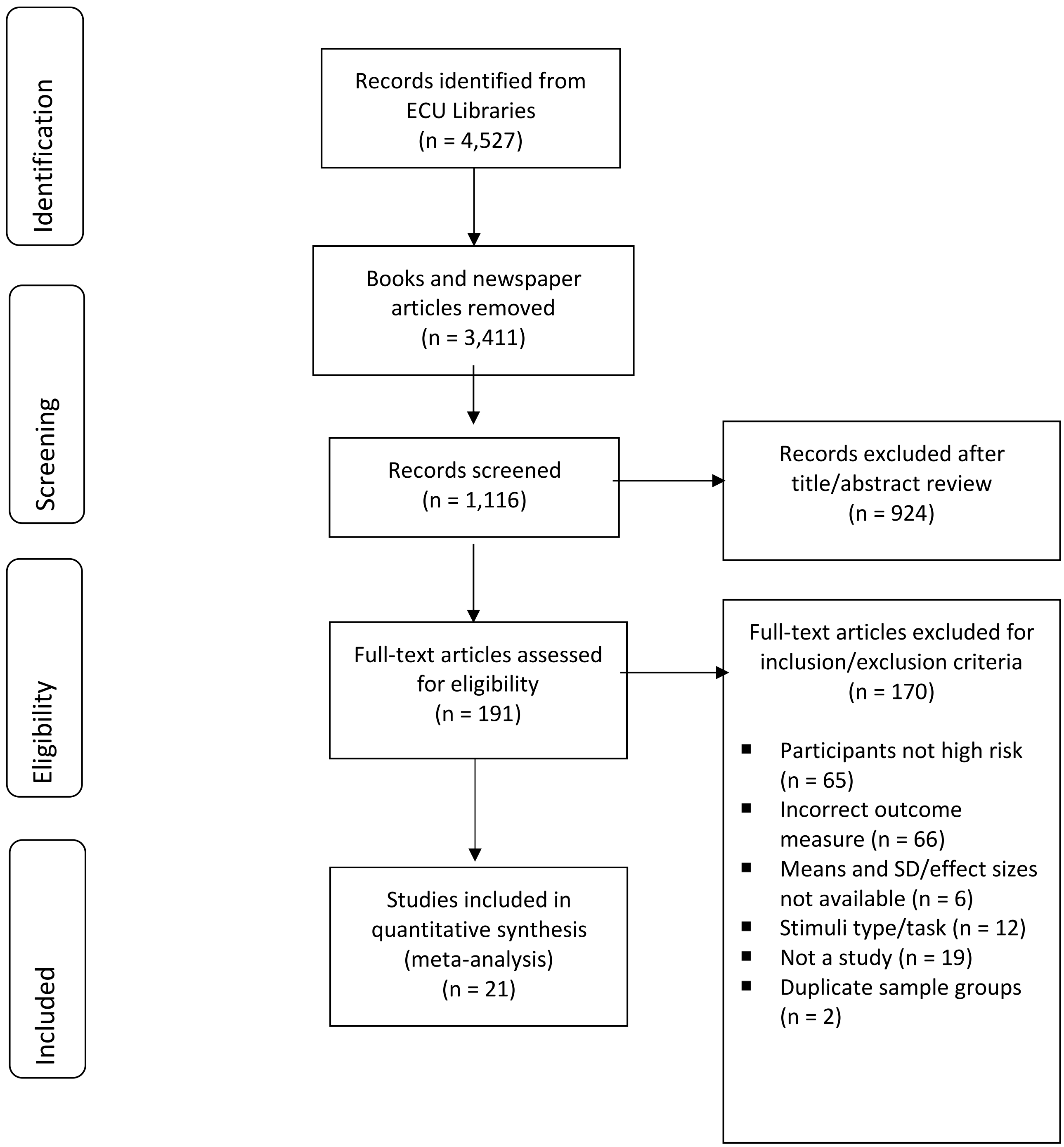

Figure 2. Forest plot of study effect sizes and confidence intervals

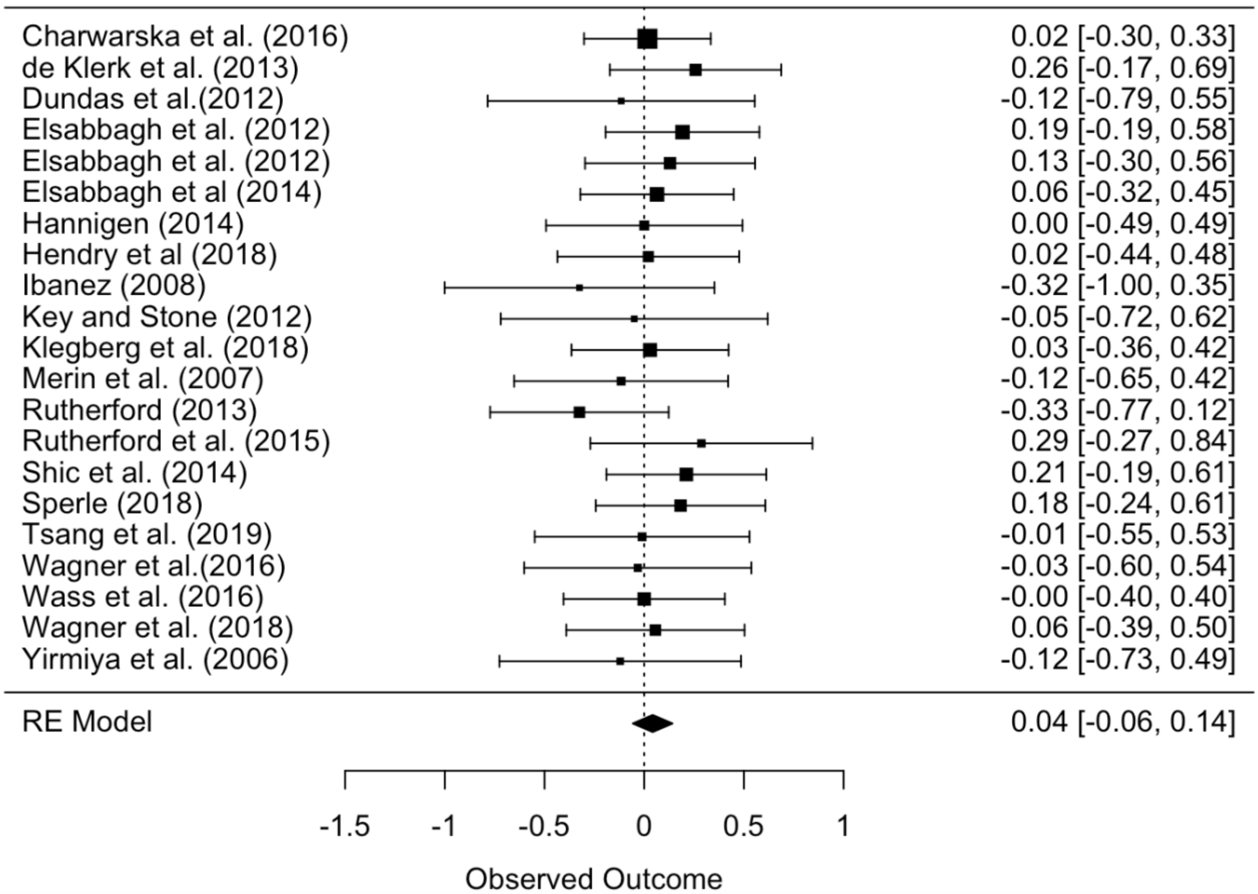

Figure 3. Funnel plot of effect sizes

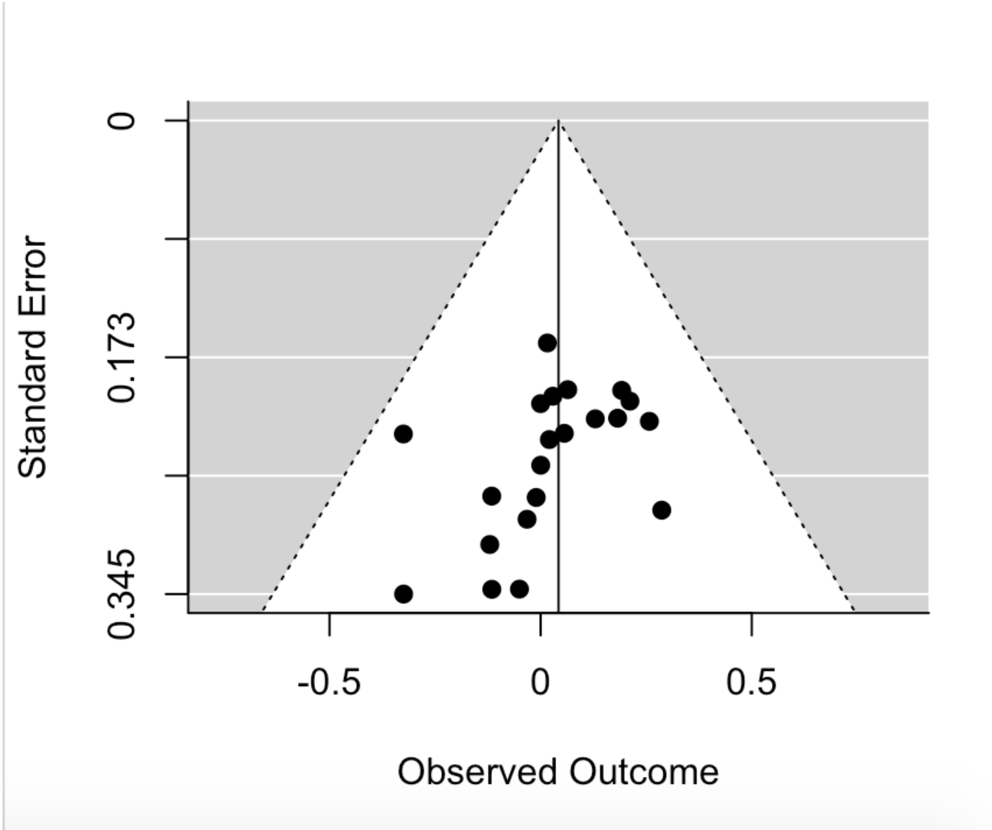

Figure 4. Boxplot of average effects by type of stimuli