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THE EARLY DEVELOPMENT OF VISUAL ATTENTIONAL MECHANISMS IN
AUTISM SPECTRUM DISORDER

A Dissertation Presented

by

HAYLEY SMITH

Submitted to the Office of Graduate Studies,
University of Massachusetts Boston,
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

May 2018

Developmental and Brain Sciences Program

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ABSTRACT

THE EARLY DEVELOPMENT OF VISUAL ATTENTIONAL MECHANISMS IN AUTISM SPECTRUM DISORDER

May 2018

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Attention plays a fundamental role in shaping cognitive development. What we attend to and what we ignore alters our visual experience of the world. Atypical attention has long been implicated in Autism Spectrum Disorder (ASD) yet our understanding of the early development of this ability has been limited by methodological factors. The aim of this thesis was to address the “toddler gap” in the literature by developing novel measures of attention that are ideal for use with toddlers, do not require verbal instructions, and can be easily scaled up or down for older or younger children. A series of three eye-tracking experiments are presented which explore visual attentional mechanisms in toddlers with ASD and age-matched typically developing controls.

Experiment 1 and Experiment 2 examined selective attention to novel task-irrelevant stimuli during visual search. Toddlers with ASD demonstrated typical

attentional capture when the task-irrelevant stimulus was defined by a novel onset, yet demonstrated atypically reduced attentional capture when the task-irrelevant stimulus was defined by a novel color. Experiment 3 examined attentional set-shifting in the context of visual search. No evidence of impaired set-shifting was found in toddlers with ASD. Together, findings provide important insights into the development of attentional mechanisms during the toddler period in ASD and in typical development.

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TABLE OF CONTENTS

| | |
|--|------|
| ACKNOWLEDGMENTS | vi |
| LIST OF TABLES | x |
| LIST OF FIGURES | xi |
| CHAPTER | Page |
| 1. INTRODUCTION | 1 |
| What is attention? | 1 |
| The networks of attention | 2 |
| Alerting/arousal..... | 3 |
| Spatial orienting..... | 3 |
| Executive control | 5 |
| Autism Spectrum Disorder | 5 |
| The diagnosis of ASD | 7 |
| Attentional differences in ASD: An introduction..... | 9 |
| Cognitive accounts of ASD and the role of attention | 10 |
| The development of attention in typically developing children | 11 |
| Attention in young children with ASD | 15 |
| Alerting/arousal..... | 15 |
| Spatial orienting..... | 17 |
| Executive control | 21 |
| The current thesis: Visual attention in toddlers with and without ASD | 22 |
| Specific Aim 1: Investigate endogenous control of attention in toddlers with and without ASD..... | 24 |
| Specific Aim 2: Investigate attentional set-shifting in toddlers with and without ASD..... | 25 |
| 2. SPECIFIC AIM 1: SELECTIVE ATTENTION IN TODDLERS WITH AND WITHOUT ASD | 26 |
| Experiment 1 | 35 |
| Methods..... | 35 |
| Participants..... | 35 |
| Apparatus | 38 |
| Stimuli..... | 38 |

| CHAPTER | Page |
|---|--------|
| Procedure | 39 |
| Data analysis | 41 |
| Results | 42 |
| Attentional priority of target during baseline search..... | 42 |
| Baseline search performance | 42 |
| Attentional priority of novel onset oddball | 43 |
| Effect of novel onset oddball on visual search | 44 |
| Discussion | 47 |
| Experiment 2 | 49 |
| Methods..... | 49 |
| Participants..... | 49 |
| Apparatus & Stimuli | 52 |
| Procedure | 52 |
| Data analysis | 53 |
| Results | 55 |
| Attentional priority of target during baseline search..... | 55 |
| Baseline search performance | 55 |
| Attentional priority of novel colored oddball..... | 56 |
| Effect of novel colored oddball on visual search..... | 57 |
| Effect of participant characteristics on attentional priority of the novel colored oddball | 61 |
| Discussion | 63 |
| General Discussion | 64 |
| 3. SPECIFIC AIM 2: ATTENTIONAL SET-SHIFTING IN TODDLERS WITH AND WITHOUT ASD | 67 |
| Experiment 3 | 71 |
| Methods..... | 71 |
| Participants..... | 71 |
| Apparatus | 74 |
| Stimuli & Procedure | 74 |
| Data analysis | 78 |
| Results | 80 |
| Training phase..... | 80 |
| Attentional set-shifting..... | 80 |
| Relations with participant characteristics | 85 |
| Discussion | 88 |

| CHAPTER | Page |
|--|------|
| 4. GENERAL DISCUSSION | 93 |
| Selective attention in toddlers with ASD | 95 |
| Executive control in toddlers with ASD | 98 |
| Visual search in toddlers with ASD | 99 |
| Limitations and future directions | 103 |
| Conclusions..... | 108 |
| REFERENCE LIST | 111 |

LIST OF TABLES

| Table | Page |
|--|------|
| 1. Summary of participants' demographic information and scores on standardized assessments in Experiment 1 | 37 |
| 2. Summary of participants' demographic information and scores on standardized assessments in Experiment 2 | 51 |
| 3. Summary of participants' demographic information and scores on standardized assessments in Experiment 3 | 73 |
| 4. Pearson's correlations between switch cost and participant characteristics in Experiment 3 | 87 |
| 5. Summary of fixation duration results from Experiment 1, 2, and 3 | 94 |
| 6. Comparison of sample characteristics and paradigm features | 101 |

LIST OF FIGURES

| Figure | Page |
|---|------|
| 1. Experiment 1 trial structure and example stimuli | 40 |
| 2. Experiment 1 hit rates (%) | 45 |
| 3. Experiment 1 average fixation durations (ms)..... | 46 |
| 4. Experiment 1 average fixation latencies (ms) during the search with oddball phase | 46 |
| 5. Experiment 1 target hit rate (%) by oddball hit rate during the search with oddball phase | 47 |
| 6. Experiment 2 trial structure and example stimuli | 53 |
| 7. Experiment 2 hit rates (%) | 58 |
| 8. Experiment 2 average fixation durations (ms)..... | 59 |
| 9. Experiment 2 average fixation latencies (ms) during the search with oddball phase | 59 |
| 10. Experiment 2 target hit rate (%) by oddball hit rate during the search with oddball phase | 60 |
| 11. Experiment 2 breakdown of hits and misses per trial during the search with oddball phase | 60 |
| 12. Relations between participant characteristics and attentional priority of the novel colored oddball in Experiment 2..... | 62 |
| 13. Experiment 3 trial structure and example stimuli | 77 |
| 14. Experiment 3 areas of interest..... | 79 |
| 15. Experiment 3 hit rates (a) and average fixation durations (b) for the T_R , the T_{IR} , and Distractors | 84 |

| Figure | Page |
|--|------|
| 16. Experiment 3 fixation latency for the T_R and the T_{IR} | 85 |
| 17. Relations between participant characteristics and SC-1 fixation duration in Experiment 3 | 88 |
| 6. Average oddball fixation duration (ms) and oddball hit rate (%) by set size in Experiment 1 and 2 | 106 |

CHAPTER 1

INTRODUCTION

What is attention?

“Millions of items of the outward order are present to my senses which never properly enter into my experience. Why? Because they have no interest for me. My experience is what I agree to attend to. Only those items which I notice shape my mind”

– James (1890)

Attention can be defined as a selective process that prioritizes a subset of information for higher-order processing (Carrasco, 2011; Petersen & Posner, 2012; Posner & Petersen, 1990). With each eye-movement, the visual system is flooded with sensory information. However, the brain is limited in its information processing capacity: neuronal activity required to process information incurs a high metabolic cost and the brain has a relatively fixed amount of energy that can be allocated to this task (Lennie, 2003). Attention provides a solution to this processing limit by biasing the brain’s resources to a specific location, object, or feature. Attended information receives enhanced representation in the brain while unattended information receives diminished representation (Desimone & Duncan, 1995).

Functionally speaking, visual attention is “the mechanism that turns looking into seeing” (Carrasco, 2011, p. 1484) — what we attend to and what we ignore alters our visual experience of the world. In some cases, the effect of attentional selection is dramatic: failing to notice a dancing gorilla while you count ball tosses, or, more serious, failing to notice a cyclist turning in front of you while you text and drive (Simons, 2000). Attention is therefore essential for efficient information processing and fundamental in shaping our experience of the world.

The networks of attention

Attention is not a single construct but rather a set of distinct yet interacting cognitive systems that are served by specific brain networks (Jiang, 2017; Raz & Buhle, 2006). Petersen and Posner describe three systems: the alerting system, the spatial orienting system, and the executive attention system (Petersen & Posner, 2012; Posner & Petersen, 1990). The structural and functional independence of these networks has been confirmed using the Attentional Networks Test (ANT) — a flanker-type task with cues — and brain imaging (Fan et al., 2009, 2012; Fan, McCandliss, Fossella, Flombaum, & Posner, 2005; Raz & Buhle, 2006). Furthermore, these networks appear to be present across the lifespan, although their efficiency and interaction changes with development (Abundis-Gutierrez, Checa, Castellanos, & Rueda, 2014; Jong, Verhoeven, Hooge, & Baar, 2016; Konrad et al., 2005; Rueda et al., 2004). In the following paragraphs, I provide an overview of each of these systems.

Alerting/arousal

The alerting system generates and maintains a state of increased arousal or vigilance (Posner, 2008). The alerting network consists of the thalamic, frontal, and parietal regions of the brain, and is influenced by the locus coeruleus-norepinephrine (LC-NE) system (Aston-Jones & Cohen, 2005). There are two components of the alerting system: tonic and phasic (Posner, 2008). Tonic alertness is often associated with ‘sustained attention’ and refers to an individual’s general level or state of wakefulness or arousal that fluctuates throughout the day (from minutes to hours). Phasic alertness, by contrast, refers to transient and short-lived changes in an individual’s levels of arousal (for example, following the abrupt appearance of a warning signal). While alerting can be distinguished from spatial orienting, real world events regularly contain information about when a target will occur (alerting) and where (orienting).

Spatial orienting

The spatial orienting system is responsible for the attentional selection of sensory information in the environment and is associated with ‘selective attention’. The orienting system consists of the superior and inferior parietal lobe, frontal eye fields, the superior colliculus of the midbrain, and the pulvinar and reticular nuclei of the thalamus (Petersen & Posner, 2012). Orienting may occur covertly (shifting attention without moving the eyes or head) or overtly (shifting attention and moving the eyes or head) (Posner, 1980).

Spatial orienting is controlled by endogenous top-down factors and exogenous bottom-up factors (Corbetta & Shulman, 2002; Jonides, 1981; Posner, 1980).

Endogenous control prioritizes selection based on current goals and is deployed voluntarily and actively. Exogenous control prioritizes selection based on perceptual salience and occurs automatically and reflexively. Events that are selected exogenously and that do not align with current goals are an example of ‘attentional capture’. While endogenous and exogenous control systems have been linked to a dorsal and ventral attention network respectively (Corbetta & Shulman, 2002; Wright & Ward, 2008), recent imaging findings suggest this mapping may be less straightforward (Corbetta, Patel, & Shulman, 2008). It is also important to note that more recently, additional attentional control factors have been proposed, including but not limited to, reward history, selection history, inter-trial priming, and emotional factors (B. A. Anderson, 2016; B. A. Anderson, Chiu, DiBartolo, & Leal, 2017; Awh, Belopolsky, & Theeuwes, 2012; Chelazzi et al., 2014; Jiang, 2017; Jiang, Swallow, Won, Cistera, & Rosenbaum, 2015; Munneke, Belopolsky, & Theeuwes, 2016). How exogenous and endogenous control systems interact in real-time is currently an area of controversy (Bacon & Egeth, 1994; Folk, Remington, & Johnston, 1992; Jonides & Yantis, 1988; Stoppel et al., 2013; Theeuwes, 2010). Nonetheless, it is generally agreed the interaction of exogenous and endogenous control systems underlie distractibility — endogenous control prioritizes selection of task-relevant information while exogenous control promotes selection of salient information regardless of task relevance.

Executive control

Executive control of attention is considered the foundation for intentional and volitional control of thoughts, emotion, and behavior. The executive control system monitors and resolves conflict between competing inputs and their responses. It recruits the lateral prefrontal cortex and the anterior cingulate (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Bush, Luu, & Posner, 2000; Cohen, 2001; Cole & Schneider, 2007; Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008; Petersen & Posner, 2012).

Three core executive control abilities have been distinguished: set-shifting (or cognitive flexibility), inhibitory control, and working memory (Diamond, 2013; Garon, Bryson, & Smith, 2008; Miyake et al., 2000). Set-shifting involves shifting from one attentional or 'mental' set to another. Inhibitory control involves suppressing a dominant response. Working memory involves the active maintenance and manipulation of information in mind.

Autism Spectrum Disorder

Autism Spectrum Disorder is a heterogeneous, neurodevelopmental disorder, that affects approximately 1 in 68 children in the US, and is approximately 4.5 times more common among males (1 in 42) than females (1 in 189) (Christensen, 2016). As many as 1 in 5 siblings of children with ASD also receive a diagnosis by age 3 (Ozonoff et al., 2011). Clinical symptoms are often first observed in early childhood, although a subset of children exhibit typical development followed by an abrupt onset of autistic symptoms with developmental regression around age two (Landa, Gross, Stuart, & Faherty, 2013).

ASD is generally believed to be lifelong, yet a minority of individuals who receive a childhood diagnosis will no longer meet clinical criteria for ASD later in life (optimal outcome) (Fein et al., 2013).

At present, the cause of ASD is unclear (Wozniak, Leezenbaum, Northrup, West, & Iverson, 2017). There is evidence that ASD has a strong genetic basis (Constantino et al., 2013), yet hundreds of genes have been implicated and no common genetic locus has emerged (State & Šestan, 2012). Many causal models agree that environmental factors interact with genes early in life causing a deviation from typical brain development (Gardener, Spiegelman, & Buka, 2009; Hallmayer et al., 2011; Hertz-Picciotto et al., 2006; M. H. Johnson, 2017; Ornoy, Weinstein-Fudim, & Ergaz, 2015). A number of pre- and peri-natal risk factors have been proposed, including maternal stress (Beverdort et al., 2005), low birth weight (Abel et al., 2013), birth complications (Ben-Ari, 2015; Zwaigenbaum et al., 2002), and premature birth (Padilla et al., 2015). Neurocognitive factors are also considered important in changing clinical outcomes (M. H. Johnson, 2012; M. H. Johnson, Gliga, Jones, & Charman, 2015; Wozniak et al., 2017). Causal accounts of ASD are further complicated by extreme heterogeneity across many aspects of the disorder, including symptom severity, symptom onset, impact on daily function, co-occurring developmental, psychiatric, neurologic, chromosomal, and genetic disorders (e.g., Attention Deficit Hyperactivity Disorder [ADHD], Obsessive-Compulsive Disorder [OCD], and Fragile X Syndrome) (Levy et al., 2010).

The diagnosis of ASD

Currently, ASD is diagnosed via behavioral assessment of two core symptom domains — socio-communicative skills and presence of restricted and repetitive interests and behaviors. Reliable diagnosis is currently possible after 14 months of age (Lord et al., 2000), however studies of infants at risk have suggested atypicalities in attentional orienting before 12 months of age may be an early behavioral marker of the disorder (Elsabbagh et al., 2013a; Gliga, Jones, Bedford, Charman, & Johnson, 2014; Jones & Klin, 2013). The present diagnostic criteria for ASD as according to the DSM-5 (American Psychiatric Association, 2013) are detailed below.

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history:

1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures: to a total lack of facial expressions and nonverbal communication.

3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.

B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history:

1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).
3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).
4. Hyper- or hypo-reactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).

- C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).
- D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.
- E. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

Attentional differences in ASD: An introduction

“There are times, more often than not, in which she is completely oblivious to all but her immediate focus of attention.”

– Kanner (1943, p. 231)

Attentional differences have long been implicated in ASD. The above quote is from Kanner who provided one of the earliest systematic descriptions of autism (for a full history of the “discovery” of autism, see Van Drenth, 2018). Although Kanner’s conclusions were based on a limited number of case studies, his writings clearly highlight an attentional profile that is distinct from the typically developing population.

Attentional differences in ASD appear to be extensive (Ames & Fletcher-Watson, 2010) — individuals with ASD demonstrate specific strengths and weaknesses,

differences are present in both social and non-social contexts, and differences do not appear to be constrained to one attentional network (discussed below). Furthermore, studies conducted with infants later diagnosed with ASD suggest that attentional differences precede the development of core symptoms and are one of the earliest behavioral indications of risk for ASD (Elsabbagh & Johnson, 2016; M. H. Johnson et al., 2015). For example, infants at high familial-risk for ASD demonstrate attentional differences to social and non-social stimuli, and, importantly, such differences are predictive of a future ASD diagnosis (Cheung, Bedford, Johnson, Charman, & Gliga, 2016; Jones & Klin, 2013; Zwaigenbaum et al., 2005a). Additionally, retrospective analyses of home video recordings of children later diagnosed with ASD suggest attentional factors involved in orienting to one's name or attending to faces are different in early development (Maestro et al., 2002; Osterling & Dawson, 1994).

Cognitive accounts of ASD and the role of attention

Given the prominence of attentional differences in ASD, as well as the importance of attention in shaping experience and cognition, atypical development of attention has been suggested to play a causal role in ASD. Early life differences in attention could have cascading consequences for cognitive development, and thus contribute to core symptoms of ASD.

Developmental cascade models of attention in ASD can be classified as domain-general accounts of ASD. Domain-general accounts posit brain-wide atypicalities and distributed impairments lead to core symptoms of ASD (Gliga et al., 2014; Keehn,

Muller, & Townsend, 2013). These developmental models of attention in ASD can be contrasted with domain-specific accounts. Domain-specific accounts posit core ASD symptoms arise from a specific impairment in a single cognitive domain, namely the ‘social brain’ (Baron-Cohen, Leslie & Frith, 1985; Chevallier, Kohls, et al., 2012; Dawson, Meltzoff, Osterling, Rinaldi & Brown, 1998; Pelphrey, Shultz, Hudac, & Vander Wyk, 2011). Deficits in social orienting, social motivation and reward networks, processing of biological movement, and theory of mind are often cited as evidence in support of domain-specific accounts.

Despite strong evidence attention may be different in ASD, empirical evidence for a link between early differences in attention and ASD is limited. In the following sections I will discuss the literature on the early development of attention in ASD. To provide context for this literature, I will begin by discussing the key findings that have emerged from the study of the typical development of attention.

The development of attention in typically developing children

As stated above, the networks of attention are present across the lifespan, yet their efficiency and interactions change with development (Abundis-Gutierrez et al., 2014; Jong et al., 2016; Konrad et al., 2005; Rueda et al., 2004). Prior to the preschool period, the alerting and orienting systems of control are the primary regulators of attention (Posner, Rothbart, Sheese, & Voelker, 2014; Rothbart & Posner, 2015). From the first weeks of life, infants show increased periods of wakefulness (Colombo, 2001), and between 2 and 6 months of age, the ability to sustain attention to a stimulus (or be in an

attentive, engaged ‘state’) improves (Reynolds & Richards, 2007; Richards, 1985; Richards & Casey, 1992). The development of the alerting system in children has been studied using a child version of the Attentional Network Test (ANT) (Rueda et al., 2004). As described previously, the ANT is a flanker-type task with spatial cues. By comparing performance across different conditions an estimate of the efficiency of each attentional network can be obtained. Alerting is assessed by measuring reaction times in the presence or absence of a warning signal. Young children have greater difficulty sustaining attention without the aid of a warning signal compared to older children and adults, and reaction times improves most rapidly during the late childhood period (Abundis-Gutierrez et al., 2014; Jong et al., 2016; Konrad et al., 2005; Rueda et al., 2004).

With regard to the spatial orienting system, the most dramatic developmental change is a shift from primarily exogenous forms of attentional control to endogenous forms of attentional control. During early infancy, orienting is primarily driven by perceptually salient information, such as contrast, or motion (Atkinson, Hood, Wattam-Bell, & Braddick, 1992; Butcher, Kalverboer, & Geuze, 2000; M. H. Johnson, Posner, & Rothbart, 1991). Endogenous control of attention during this period is rudimentary: for example, 8-month-old but not 6-month-old infants are able to voluntarily disengage attention from a salient dynamic stimulus in order to receive a reward at a less salient location (Tummeltshammer, Mareschal, & Kirkham, 2014). However, this form of attentional control is fundamental for arousal regulation during infancy, enabling infants to shift attention away from events that are distressing or overstimulating (Rothbart,

Sheese, Rueda, & Posner, 2011). Endogenous control of attention clearly improves during early childhood, however, task-irrelevant stimuli are more likely to automatically capture attention and thus detract resources from the task at hand compared to adults. Increased distractibility in children has demonstrated in the laboratory as well as in a classroom settings (Fisher, Godwin, & Seltman, 2014; Gaspelin, Margett-Jordan, & Ruthruff, 2014; Rothbart & Posner, 2015; Wolf & Pfeiffer, 2014). It is not until late childhood or adolescence that voluntary endogenous control of attention reaches adult-like levels (Enns & Akhtar, 1989; Kramer, de Sather, & Cassavaugh, 2005; Pasto & Burack, 1997; Ristic & Kingstone, 2009; Rueda et al., 2004).

Although less robust endogenous control of attention during early childhood may increase distractibility, it may also be adaptive, ensuring young children do not miss potentially important opportunities for learning about the world (Plebanek & Sloutsky, 2017; Tighe, Glick, & Cole, 1971). In adulthood, as attention is under more robust endogenous control, information that is not within the attentional set is often ignored, even if this information is, in fact, relevant (Bacon & Egeth, 1994; Folk et al., 1992; Jonides & Yantis, 1988; Stoppel et al., 2013; Theeuwes, 2010).

During the childhood period, visual search for a feature-conjunction target also improves with age (Donnelly et al., 2007; Gerhardstein & Rovee-Collier, 2002; Hommel, Li, & Li, 2004; Trick & Enns, 1998; Woods et al., 2013). Feature-conjunction search requires guiding search in accordance with a pre-defined target template (so-called effortful search) (Treisman & Gelade, 1980; Wolfe & Horowitz, 2004, 2017). The

similarity of the target to distractors minimizes the utility of exogenous attentional control and therefore often depends primarily on endogenous control (Wolfe, Butcher, Lee, & Hyle, 2003).

Executive control of attention follows the most protracted developmental course of the three attentional systems (Best & Miller, 2010; Diamond, 2013; Garon et al., 2008; Zelazo, 2004). During the second half of the first year, infants are increasingly capable of manipulating one to two object representations in mind, depending on object complexity (Kaldy, Guillory, & Blaser, 2015; Kaldy & Leslie, 2003, 2005; Ross-Sheehy, Oakes, & Luck, 2003). They also are able to maintain a representation of a hidden toy in mind and inhibit a tendency to search for that object at previous hiding location (Diamond & Goldman-Rakic, 1989). During the preschool period, children become increasingly able to hold conflicting rules in mind and flexibly shift attention between those rules (Garon et al., 2008; Hendry, Jones, & Charman, 2016). For example, on standard versions of the Dimensional Change Card Sort (DCCS) (Frye, Zelazo, & Palfai, 1995) most children aged 3 show difficulty switching to a new rule that conflicts with the initially learned rule (or 'mental set') and instead persevere, that is, continue to implement the initial rule (for alternative ways children err, see Chevalier & Blaye, 2008). By contrast, most children aged 4-5 switch rules with ease (for a review, see Doebel & Zelazo, 2015). Working memory also appears to improve in capacity during childhood, although capacity estimates during this period vary widely and depend heavily on the type of assessment employed (Cowan, 2016; Fitch, Smith, Guillory, & Kaldy, 2016).

Attention in young children with ASD

In the following section, I will describe the key findings on the development of the attention networks from infancy to childhood in ASD. I will provide evidence of typical and atypical functioning within the alerting, spatial orienting, and executive attention network. It is worth noting, however, it has recently been suggested that attentional differences arise from atypicalities in the interaction of the attention networks in addition to or instead of localized atypicalities within each of the attention networks (Fan et al., 2012; Farrant & Uddin, 2016). For example, Using the Attentional Network Test, Keehn et al. (2010) found that children with ASD showed more dependence between the alerting and spatial orienting systems, as well as a specific impairment in spatial orienting. Thus, in addition to within network differences, individuals with ASD may also demonstrate differences in network connectivity.

Alerting/Arousal

Atypical functioning of the alerting system of attention has been hypothesized to be linked to multiple aspects of ASD, including hyper- and hypo-arousal, sensory dysfunction, and over-selective attention (Dawson & Lewy, 1989; Hutt, Hutt, Lee, & Ounsted, 1964; Keehn et al., 2013; Liss, Saulnier, Fein, & Kinsbourne, 2006; Rogers & Ozonoff, 2005).

Only a handful of studies have examined alerting in young children with ASD, and these studies have used task-evoked pupil responses (C. J. Anderson & Colombo, 2009; C. J. Anderson, Colombo, & Shaddy, 2006; Blaser, Eglington, Carter, & Kaldy,

2014; Martineau et al., 2011). The task-evoked pupil response is controlled by the LC-NE system and thus can serve as a biomarker of the alerting network (Koss, 1986; Laeng, Sirois, & Gredeback, 2012; Samuels & Szabadi, 2008). Anderson, Colombo, and others, for example, found that children with ASD demonstrate increased tonic baseline pupillary response (C. J. Anderson & Colombo, 2009; Christa J. Anderson, Colombo, & Unruh, 2013) as well as atypically reduced phasic responding to faces (C. J. Anderson et al., 2006). More recently, Blaser et al. (2014) found that toddlers with ASD show an increased tonic baseline pupillary response as well as atypically increased phasic responding to a visual search target, which the authors interpret as evidence of increased cognitive effort during search and a potential explanation for the visual search advantage. Event-related potentials (ERPs) related to detection of novel or unexpected stimuli have also been shown to be atypical in children with ASD. For example, unattended auditory stimuli elicit reduced N1c and P100 amplitudes in the right hemisphere in children with ASD and this response is related to the degree of developmental delay and sensory difficulties (Orehova et al., 2009; Stroganova et al., 2013).

In addition to atypical tonic levels of arousal, regulation of this system in different contexts may be atypical. However research on this particular subject has only been conducted with older children. Gomot and others recorded the BOLD responses of high-functioning children with ASD while performing auditory oddball task. During *passive* auditory oddball detection (children watched a silent movie while being played sounds), children with ASD demonstrate hypo-responsivity: reduced activation in the left anterior

cingulate cortex, bilateral temporoparietal region, and right inferior and middle frontal areas relative to typically developing (TD) children (Gomot et al., 2006)¹. By contrast, during *active* auditory oddball detection, children with ASD demonstrated hyper-responsivity: increased activation in the right prefrontal-premotor and the left inferior parietal regions as well as faster reaction times (Gomot, Belmonte, Bullmore, Bernard, & Baron-Cohen, 2008). Despite evidence of atypical tonic alerting, behavioral measures of sustained attention in children have suggested this aspect of attention is typical (Garretson, Fein, & Waterhouse, 1990; K. A. Johnson et al., 2007).

Thus, while there appears to be empirical evidence that alerting network is atypical in the young children with ASD, the limited number of studies investigating this system has prevented clear answers regarding whether this network is impaired or not. Furthermore, the possibility of subtypes of ASD has complicated study of this system — individuals with ASD may either be hyper-aroused or hypo-aroused.

Spatial orienting

Spatial orienting in infants and young children with ASD has primarily been investigated using paradigms that elicit exogenous stimulus-driven control of attention (M. H. Johnson et al., 2015). The gap-overlap task is one paradigm that has been used extensively (Reulen, 1984a, 1984b; Reuter-Lorenz, Hughes, & Fendrich, 1991; Saslow, 1967). In this task, attentional disengagement from a central stimulus in response to the onset of a peripheral stimulus is measured via eye-tracking. Disengagement cost is

¹ As there was no active task, no behavioral response was measured.

computed by comparing the difference in saccadic latency to a peripheral stimulus appearing *after* the central stimulus has disappeared (shift trials) to saccadic latency to a peripheral stimulus appearing *while* the central stimulus is still present (disengage trials). Evidence of slower attentional disengagement in this task is often cited as evidence of a domain-general deficit in spatial orienting in ASD (Elsabbagh & Johnson, 2016; Sacrey, Armstrong, Bryson, & Zwaigenbaum, 2014). Restricted interests and repetitive behaviors, such as spinning a wheel on a toy car, are a core feature of ASD that could stem from ‘sticky’ attention, while impairments in moving attention around the world could dramatically change how children experience the world, with cascading consequences for social development.

Impaired attentional disengagement has been reported in young infants at high familial risk for ASD (Elsabbagh et al., 2013b; Zwaigenbaum et al., 2005b). For example, Elsabbagh et al. (2013) reported poorer disengagement at 14, but not at 7 months of age. However, we recently found no evidence of an ASD impairment in this task in a large sample of 2-year-old toddlers (Fischer et al., 2016, Robertson, et al., under review), replicating a previous finding from 5-12-year-old children with ASD (Fischer, Koldewyn, Jiang, & Kanwisher, 2013). A closer inspection of the literature reveals that the empirical evidence for impaired disengagement in ASD may be weak. For example, a recent review of the literature reported almost a quarter of published studies found no evidence of an ASD impairment (Sacrey et al., 2014). Furthermore, stimulus repetition as well as stimulus salience (e.g. dynamic, multi-modal, etc), appears to be relevant in determining

whether disengagement is typical, suggesting this effect could be driven by stimulus- or task-specific factors (Sabatos-DeVito, Schipul, Bulluck, Belger, & Baranek, 2016).

Free-viewing visual-exploration tasks have also been used to study exogenous orienting in infants and children with ASD (Elison, Sasson, Turner-Brown, Dichter, & Bodfish, 2012; Gliga, Smith, Lively, Charman, & Johnson, 2015; T. J. Heaton & Freeth, 2016; Pellicano et al., 2011; Sasson, Elison, Turner-Brown, Dichter, & Bodfish, 2011; Sasson, Turner-Brown, Holtzclaw, Lam, & Bodfish, 2008; Wass et al., 2015). Here the findings have been mixed. Wass et al. (2015), for example, reported low-risk infants demonstrated longer fixation durations than high-risk infants (aged 6 to 9 months), and fixation durations were the shortest in infants who eventually received a clinical diagnosis of ASD at 36 months. By contrast, Sasson et al. (2011) reported longer fixation durations and more circumscribed exploration of a visual scene in children aged between 2 and 5 with ASD compared to TD age-matched controls. The latter finding is similar to that of Gliga et al. (2015). Eight-month-old infants at high-risk for ASD were presented with visual scenes and gaze patterns were recorded. Infants who demonstrated low levels of hyperactivity showed more circumscribed exploration and a larger number of revisits than infants who showed high levels of hyperactivity (a behavioral profile associated with high risk for ADHD).

A very limited number of studies have investigated endogenous control of attention young children. The lack of studies on this aspect of attention is primarily due to methodological reasons — young children do not reliably follow instructions and so

getting them to control attention in a specific goal-directed manner can be difficult.

However, one method that has been used successfully is visual search (Kaldy, Giserman, Carter, & Blaser, 2011; Gliga, Bedford, et al., 2015).

Visual search is a classic paradigm in visual psychophysics. This laboratory task captures a typical everyday situation where selective attention is required: localizing objects in cluttered visual scenes. Some visual search tasks are trivially easy and do not require effort, for instance, finding a red circle amidst a field of green circle distractors; referred to as single-feature search, where the target ‘pops-out’ by virtue of its unique feature (i.e., color). Some are more difficult, for instance, finding that same red circle, but now amidst blue circles and red squares; referred to as feature-conjunction search where more effortful, deliberate search is required as set size increases (Treisman & Gelade, 1980; Wolfe & Horowitz, 2004, 2017). Importantly, in complex scenes visual search (as is often the case in feature-conjunction search) attention must be guided voluntarily and in accordance with a search goal (Eckstein, 2011; Eimer, 2014; Wolfe et al., 2003).

Kaldy et al. (2011) developed a novel visual search paradigm that utilizes eye-tracking rather than a manual response and relies on a cue-reward animation to encourage children to search for the target rather than verbal instructions. They found that even 2-year-old toddlers with ASD were more successful than age-matched TD controls, by up to a factor of two, at fixating the target. This finding supports a robust literature that visual search is an area of strength in ASD — across a wide range of ages, individuals

with ASD have been found to both faster and more successful than TD controls at this task (for a review, see Kaldy, Giserman, Carter, & Blaser, 2013; Simmons et al., 2009).

It is important to note that although feature-conjunction visual search depends on endogenous control of attention, visual search is a complex task. Thus, whether the visual search advantage in ASD arises primarily from differences in attentional control is unclear. Dominant accounts of the visual search advantage include enhanced low-level perceptual processing (Happe & Frith, 2006; Joseph, Keehn, Connolly, Wolfe, & Horowitz, 2009; Mottron, Dawson, Soulières, Hubert, & Burack, 2006; Shira, Kato, & Kashino, 2017), greater perceptual capacity (Hessels, Hooge, Snijders, & Kemner, 2014; Remington, Swettenham, Campbell, & Coleman, 2009), and increased attentional efficiency or focused attention (Blaser et al., 2014; Milne, Dunn, Freeth, & Rosas-Martinez, 2013)

Executive control

As discussed above, executive control involves set-shifting, inhibitory control, and working memory. The majority of studies conducted with young children have focused on complex set-shifting, which also recruits inhibitory control and working memory (although a handful of studies have documented early impairments in spatial working memory; for examples see: Garon, Smith, & Bryson, 2017; Jiang, Capistrano, & Palm, 2014; Pellicano et al., 2017). Studies employing complex attentional set-shifting paradigms (such as the DCCS) in preschool-aged children diagnosed with ASD suggest that the development of executive control in this population is delayed: preschoolers with

ASD make more perseverative errors and take longer to reach criterion following a switch compared to chronologically age-matched TD controls (Garon, Smith, & Bryson, 2017; Kimhi, Shoam-Kugelmas, Ben-Artzi, Ben-Moshe, & Bauminger-Zviely, 2014; Pellicano et al., 2017; Pellicano, Maybery, Durkin, & Maley, 2006) and mental age-matched TD controls (McEvoy, Rogers, & Pennington, 1993). On the other hand, studies employing simpler response shifting paradigms (such as the A-not-B task, Piaget, 1954; or the Spatial Reversal task, Kaufman, Leckman, & Ort, 1989) suggest deficits in executive control are not a primary factor in the development of behavioral inflexibility in young children diagnosed with ASD: preschoolers with ASD performed equivalently to chronologically age-matched TD controls (Dawson et al., 2002; Griffith, Pennington, Wehner, & Rogers, 1999; Yerys, Hepburn, Pennington, & Rogers, 2007). To date, no studies have measured attentional set-shifting young children with ASD. Thus it is unclear whether set-shifting per se is impaired early in development, or only complex attentional-set shifting is impaired in ASD.

The current thesis: Visual attention in toddlers with and without ASD

Research into the typical and atypical development of attention during toddler period has been limited by methodological constraints: toddlers pose a measurement problem — too old for looking-based measures of attention that are regularly used with infants, yet too young to reliably follow verbal instructions or pay attention for long periods of time, as required by measures of attention used with children.

An improved understanding of how attention develops during the toddler period would greatly improve characterization of the emergence of ASD. Although certain behavioral symptoms of ASD have been documented prior to the second year of life (Osterling & Dawson, 1994; Wolff et al., 2014; Zwaigenbaum et al., 2005a) reliable diagnosis is currently only possible by toddlerhood (Brian et al., 2008). By studying children at the earliest age ASD can be diagnosed, we can understand attentional development when it is still independent of the effects of behavioral or pharmacological intervention. Furthermore, an understanding of the attentional strengths and weaknesses of toddlers with ASD would improve options for the development of new early intervention programs that can either address areas of concern or capitalize upon areas of competence, and, ultimately, reduce ASD-related symptoms later in life (Bryson, Rogers, & Fombonne, 2003; Dawson, 2008; Wallace & Rogers, 2010; Zwaigenbaum et al., 2015).

There were two primary goals of the present thesis. First, we wanted to address the toddler gap in the ASD attention literature. Participants were toddlers (~18 to 36 months) just-diagnosed with ASD and typically developing (TD) chronologically age-matched toddlers. We developed a series of novel eye-tracking tasks which enable measurement of attention without the need for manual response or verbal instructions. Second, we wanted to address limited scope in study of the early development of attention by examining aspects of attention that have previously been understudied.

Specific Aim 1: Investigate endogenous control of attention in toddlers with and without ASD

Developmental accounts of ASD, in particular, have suggested that altered maturation of the attentional systems could dramatically change how young children experience their world, with cascading consequences for cognitive development (Bedford et al., 2014; Elsabbagh & Johnson, 2016; M. H. Johnson, 2014; Keehn et al., 2013). Currently, our understanding of the development of selective attention in ASD has been informed primarily by tasks that measure exogenous stimulus-driven orienting in ‘task-free’ passive viewing contexts (M. H. Johnson et al., 2015). Selective attention in the real-world regularly involves the interaction of exogenous and endogenous goal-driven control processes and thus it is important to understand the development of attention in a context where both forms of attentional control interact.

In Experiments 1 and 2, we investigated endogenous control to a novel task-irrelevant oddball during visual search in toddlers diagnosed with ASD (Experiment 1: $N = 30$; Experiment 2: $N = 34$) and chronological age-matched TD controls (Experiment 1: $N = 34$; Experiment 2: $N = 36$). Furthermore, there is evidence selective attention in ASD may demonstrate stimulus-specific atypicalities (Greenaway & Plaisted, 2005; Keehn & Joseph, 2008; Keehn, Nair, Lincoln, Townsend, & Muller, 2016; Keehn, Westerfield, Muller, & Townsend, 2017). Thus, in Experiment 1, we investigated the effect of a novel *onset* oddball, and, in Experiment 2, we investigated the effect of a novel *colored* oddball.

Specific Aim 2: Investigate attentional set-shifting in toddlers with and without ASD

The development of executive control is necessary for flexible and voluntary control of behavior. Deficits in executive control are claimed to be a primary cause of behavioral inflexibility — a core clinical symptom — in ASD. Attentional set-shifting has traditionally been measured with the Wisconsin Card Sort Task, however, this task requires following verbal instructions. In Experiment 3, we developed a novel visual search task to test attentional set-shifting in toddlers diagnosed with ASD ($N = 29$) and chronological age-matched TD controls ($N = 30$). On each trial, a relevant and an irrelevant target were embedded amongst a set of feature-conjunction distractors and toddlers were tasked with searching for the relevant target. Critically, after a set of trials the relevant and irrelevant targets reversed (i.e., the previously relevant target became irrelevant, and the previously irrelevant target became relevant).

CHAPTER 2

SPECIFIC AIM 1: SELECTIVE ATTENTION IN TODDLERS WITH AND WITHOUT ASD

Attention biases information processing resources to a location, object, or feature (Desimone & Duncan, 1995; Petersen & Posner, 2012). Attended information receives enhanced representation in the brain while unattended information is ignored. Given the vast amount of visual information available for selection, adaptive functioning requires focusing attentional resources on relevant information. At times, this may mean detecting and attending to relevant events that occur outside our current focus of attention. For example, the sudden appearance of a shadow in our periphery might signal danger, or the appearance of a novel object could suggest an opportunity for exploration and learning.

Selection of sensory information is determined by endogenous top-down factors and exogenous bottom-up factors (Corbetta & Shulman, 2002; Jonides, 1981; Posner, 1980). Endogenous control prioritizes selection based on current goals and is deployed voluntarily and actively. Exogenous control prioritizes selection based on perceptual

saliency and occurs automatically and reflexively. In typically developing (TD) individuals, exogenous control over selective attention matures earlier than endogenous control (Colombo & Cheatham, 2006; Ristic & Enns, 2015; Ruff & Rothbart, 2001). For example, during infancy, orienting is primarily in response to perceptually salient information, such as contrast, or motion (Atkinson et al., 1992; Butcher et al., 2000; M. H. Johnson et al., 1991). During childhood, endogenous control of attention improves yet children demonstrate increased susceptibility to distraction relative to adults (Fisher et al., 2014; Gaspelin et al., 2014; McDermott, Perez-Edgar, & Fox, 2007; Rothbart & Posner, 2015; Rueda et al., 2004; Wolf & Pfeiffer, 2014). For example, kindergarten children spend less time off-task and show better learning outcomes when learning occurs in a ‘minimalist’ classroom (i.e., no visual content on walls) compared to when learning occurs in a ‘standard’ classroom (i.e., visual content on walls).

Autism Spectrum Disorder (ASD) is primarily characterized by deficits in socio-communicative skills as well as restricted and repetitive behaviors and interests. However, differences in selective attention have increasingly been implicated in the etiology of this disorder. Developmental accounts of ASD, in particular, have suggested altered maturation of the attentional systems could dramatically change how young children experience their world, with lasting consequences for cognitive development more generally (Elsabbagh & Johnson, 2016; M. H. Johnson, 2017; M. H. Johnson et al., 2015; Keehn et al., 2013).

The early development of selective attention in ASD has primarily been investigated using paradigms that elicit exogenous stimulus-driven control of attention (M. H. Johnson et al., 2015). One paradigm that has been used extensively is the gap-overlap task (Reulen, 1984a, 1984b; Reuter-Lorenz et al., 1991; Saslow, 1967). In this task, attentional disengagement from a central stimulus in response to the onset of a peripheral stimulus is measured via eye-tracking. Disengagement cost is computed by comparing the difference in saccadic latency to a peripheral stimulus appearing *after* the central stimulus has disappeared (shift trials) to saccadic latency to a peripheral stimulus appearing *while* the central stimulus is still present (disengage trials). Evidence of slower attentional disengagement in this task is often cited as evidence of a domain-general deficit in spatial orienting in ASD (Elsabbagh & Johnson, 2016; Sacrey et al., 2014). Restricted interests and repetitive behaviors, such as spinning a toy car wheel, are a core feature of ASD that could stem from ‘sticky’ attention, while impairments in moving attention around the world could dramatically change how children experience the world, with cascading consequences for social development.

However, empirical evidence for impaired disengagement in ASD is actually quite weak. We recently found no evidence of an ASD impairment in a large sample of toddlers (Fischer et al., 2016; Robertson et al., under review), replicating a previous finding from children with ASD (Fischer et al., 2013). Furthermore, a recent review of the literature reported almost a quarter of published studies found no evidence of an ASD impairment (Sacrey et al., 2014). Task-specific factors may account for the mixed findings: stimulus

repetition as well as stimulus salience (e.g., dynamic, multi-modal, etc), appear to be relevant in determining whether disengagement is typical (Sabatos-DeVito et al., 2016), therefore leading one to question the extent of the disengagement deficit in ASD.

Free-viewing visual-exploration tasks have also been used to study the early development of selective attention in ASD (Elison et al., 2012; Gliga, Smith, et al., 2015; T. J. Heaton & Freeth, 2016; Pellicano et al., 2011; Sasson et al., 2011, 2008; Wass et al., 2015). Here the findings have been mixed. Wass et al. (2015), for example, reported low-risk infants demonstrated longer fixation durations than high-risk infants (aged 6 to 9 months), and fixation durations were the shortest in infants who eventually received a clinical diagnosis of ASD at 36 months. By contrast, Sasson and others (2011) reported longer fixation durations and more circumscribed exploration of a visual scene in children aged between 2 and 5 years with ASD compared to TD age-matched controls. The latter finding is similar to that of Gliga et al. (2015), who reported 8-month-old infants at high-risk for ASD with low levels of hyperactivity (low risk for ADHD) showed more circumscribed exploration of a visual scene and more item re-visits than infants at high-risk for ASD with high levels of hyperactivity (a behavioral profile associated with high risk for ADHD).

A very limited number of studies have investigated endogenous control of attention young children. The lack of studies on this aspect of attention is primarily due to methodological reasons — young children do not reliably follow instructions and so

getting them to control attention in a specific goal-directed manner can be difficult.

However, one method that has been used successfully is visual search.

Visual search is a classic paradigm in visual psychophysics, and an ASD advantage has been found in toddlers, school-age children, and adults with ASD as well as infants at high-familial risk for ASD (Gliga, Bedford, et al., 2015; Kaldy et al., 2011; Plaisted, O'Riordan, & Baron-Cohen, 1998). Single-feature visual search is efficient and does not require effort as the target 'pops-out' by virtue of its unique feature (e.g., a red circle target amongst a homogenous set of blue circles). Feature-conjunction visual search is inefficient and effortful as the target is defined by a conjunction of features (e.g., a red circle target amongst blue circles and red squares) (Treisman & Gelade, 1980; Wolfe & Horowitz, 2004, 2017). Given the complexity of the visual scene, feature-conjunction search minimizing the contribution of exogenous control and instead requires guiding attention voluntarily and in accordance with a search goal (Eckstein, 2011; Eimer, 2014; Wolfe et al., 2003).

In a recent study, Kaldy et al. (2011) found that toddlers with ASD were more successful than age-matched TD controls at visual search. This finding supports a robust literature that visual search is an area of strength for individuals with ASD — across a wide range of ages, individuals with ASD have been found to both faster and more successful than TD controls at this task (for a review, see Kaldy, Giserman, Carter, & Blaser, 2013; Simmons et al., 2009). In Kaldy et al. (2011), toddlers were tasked with searching for a red apple target amongst a set of blue apple and red oblong distractors.

The target was cued prior to search and animated at the end of the search period.

Importantly, this task did not require verbal instructions, making it ideal for examining endogenous control of attention with toddlers with weak language skills.

The limited scope of the study of selective attention in young children with ASD is a major barrier in our understanding of the link between early differences in attention the development of core symptoms of ASD. An improved understanding of how attention develops during the toddler period would greatly improve characterization of the emergence of ASD as well as improve options for the development of new early intervention programs that can either address areas of concern or capitalize upon areas of competence, and, ultimately, reduce ASD-related symptoms later in life (Bryson, Rogers, & Fombonne, 2003; Dawson, 2008; Wallace & Rogers, 2010; Zwaigenbaum et al., 2015).

In the present study, we use a similar approach to Kaldy et al. (2011) to investigate selective attention to a novel task-irrelevant oddball in toddlers just-diagnosed with ASD and chronologically age-matched TD controls (age range: 17 – 36 months). Toddlers were tasked with searching for a red apple target among feature-conjunction distractors (blue apples and red oblong shapes). After a series of baseline trials, a novel oddball was introduced into the search array. Rather than a manual or a verbal response, we measured gaze behavior via eye-tracking; a rich measure of selective attention. Selective attention in the real world regularly involves focusing attentional resources on relevant information while ignoring irrelevant information. By the first year of life, typically developing infants are already beginning to guide attention voluntarily and in

accordance with their current goals or expectations (Rothbart & Posner, 2015; Rothbart et al., 2011; Ruff & Rothbart, 2001). It therefore important to consider the development of selective attention in ASD in contexts where exogenous and endogenous systems interact.

Research with older children and adults has suggested that individuals with ASD show atypical allocation of attention. In certain contexts, selective attention in ASD can be overly selective, narrow, or over-focused (Behrmann, Thomas, & Humphreys, 2006; Happe & Frith, 2006; Robertson, Kravitz, Freyberg, Baron-Cohen, & Baker, 2013). For example, children and adults with ASD demonstrate reduced sensitivity to unexpected novel stimuli in an oddball paradigm when attention is directed elsewhere; a finding that could be explained by an atypically narrow focus of attention (Gomot et al., 2006; Liss et al., 2006; Orekhova & Stroganova, 2014). Deficits in modulating the size of the attentional spotlight have also been documented (Burack, 1994; Mann & Walker, 2003; Ronconi, Gori, Ruffino, Molteni, & Facoetti, 2013). For example, Ronconi et al. (2013) measured children's reaction times in response to a target presented at small or large eccentricities from a central fixation. Critically, when a small spatial cue was presented, both children with ASD and TD were equally fast to respond to the target. However, when a large spatial cue was presented, children ASD demonstrated longer response times, leading the authors to suggest the zoom-out mechanisms of attention in ASD is slow or 'sluggish'.

In other contexts, individuals with ASD show increased distractibility and increased attentional modulation by task-irrelevant information. For example, older

children with ASD demonstrate slower responding on incongruent trials in flanker-type tasks (Adams & Jarrold, 2012; Christ, Holt, White, & Green, 2007) and greater attentional capture by cues occurring in a task-irrelevant modality (Murphy, Foxe, Peters, & Molholm, 2014). It has been suggested this may arise from a greater perceptual capacity, that is, an ability to process more perceptual information before some critical limit is reached (Ohta et al., 2012; Remington et al., 2009; Swettenham et al., 2014).

Finally, there is evidence atypical allocation of attention depends on stimulus properties. Previous research has suggested older children and adults with ASD show impaired attentional modulation by novel onset stimuli (Greenaway & Plaisted, 2005; Keehn & Joseph, 2008). Greenaway and Plaisted (2005) reported attentional capture by a novel onset item was reduced in children with ASD, regardless of task-relevance, leading the authors to propose that a domain-general impairment in processing dynamic stimuli is one feature of ASD. A similar finding was reported by Keehn and Joseph (2008) using a preview visual search paradigm — children with ASD were less affected by the delayed onset of the second half of the visual search array.

Attentional capture to task-relevant and task-irrelevant colored stimuli may or may not be typical in ASD. For example, Greenaway and Plaisted (2005) found that attentional modulation by a colored oddball when task-relevant (i.e., a valid cue) or task irrelevant (i.e., a visual search distractor) was typical in older children with ASD. By contrast, adolescents and young adults with ASD demonstrated superior target detection when a distractor shared a color with the target — a color facilitation effect not observed

in TD controls (Brian, Tipper, Weaver, & Bryson, 2003). Recently, Keehn and others used to neuroimaging to investigate attention to colored stimuli in children with and without ASD (Keehn et al., 2016, 2017). Participants were required to detect a colored target embedded amongst distractors in rapid serial presentation task. Critically, distractors were either neutral (grey), task-relevant (i.e., the same color as the target), or were task-irrelevant (i.e., a novel color). TD children demonstrated robust attentional capture by targets as well as increased attentional capture by relevant distractors compared to irrelevant distractors. By contrast, children with ASD showed reduced attentional capture for both targets and distractors, regardless of task-relevance.

In Experiment 1, we asked whether a novel onset oddball (appearing 300 ms after the search array onset) would capture attention. In Experiment 2, we asked whether a novel colored oddball would capture attention. We considered three potential outcomes in terms of differences between the TD and ASD toddlers: (1) toddlers with ASD will show reduced attentional capture by the novel oddball, potentially the result of over-focused attention (e.g. Gomot et al., 2006) ; or, on the contrary (2) toddlers with ASD will show increased attentional capture by the novel oddball, potentially the result of an inability to filter out irrelevant information (e.g. Murphy et al., 2014); and in addition to this, (3) attentional capture in ASD will be stimulus specific.

Experiment 1

Here we examined how the introduction of a novel onset oddball during conjunction visual search affects attention allocation in toddlers just diagnosed with ASD and TD chronologically age-matched controls.

Methods

Participants

Children with TD were recruited from the Greater Boston area via mailings. Children diagnosed with ASD were recruited through local early intervention agencies and participation occurred at the beginning of the visit in which diagnostic testing was later performed. Following the experimental procedure, the general cognitive functioning of all children was assessed using the Mullen Scales of Early Learning (MSEL; Mullen & others, 1995). For children with ASD, clinical diagnosis was assigned by a licensed psychologist using the Autism Diagnostic Observation Schedule-2 (Lord, Rutter, et al., 2012; Lord, Luyster, Gotham, & Guthrie, 2012) (Toddler Module, $N = 22$; Module 1, $N = 7$; Module 2, $N = 1$). Calibrated severity scores (CSS) were calculated using the method described by Esler et al. (2015) (Toddler Module) and Hus et al. (2014) (Module 1 and 2). For children with TD, we verified that no participant had a history of neurological disorders, developmental issues, ASD behaviors, or siblings with developmental disorders via parental report. Typical development was determined using the Early Learning Composite standard score (ELC) on the MSEL and scores on the Brief Infant–Toddler Social and Emotional Assessment (BITSEA) (Briggs-Gowan, Carter, Irwin,

Wachtel, & Cicchetti, 2004). An ELC on the MSEL below 70 is 2 SD below the standardized mean and equivalent to a “well below average” level of cognitive development. Children who did not meet criteria for TD (2 children) or for ASD (8 children) were excluded. Participants had no known vision impairments or first-degree relatives with colorblindness (1 ASD child excluded).

Thirty-six TD children and thirty-five children diagnosed with ASD were tested. Nine of these children were excluded because of poor eye-track quality (2 TD, 7 ASD). None of the children failed to meet the minimum valid trial criterion (see Data Analysis). The final participant sample was 34 children with TD and 30 children diagnosed with ASD. Participants’ were matched in chronological age (TD: $M = 26.18$, $SD = 5.91$; ASD: $M = 27.43$, $SD = 4.97$). Table 1 shows a summary of participants’ demographic information and assessment scores.

Table 1. Summary of participants' demographic information and scores on standardized assessments in Experiment 1.

| | ASD | TD |
|------------------------|---------------|---------------|
| N | 30 | 34 |
| # Females | 8 | 11 |
| Age (months) | 27.43 (4.97) | 26.18 (5.91) |
| range | 16.91 - 36.55 | 18.13 - 35.92 |
| Valid trials collected | 14.17 (2.80) | 13.88 (2.48) |
| Ethnicity (# children) | | |
| Hispanic or Latino | 6 | 5 |
| Not Hispanic or Latino | 24 | 29 |
| Mullen Scales: | | |
| VR | 30.00 (10.88) | 55.97 (14.55) |
| FM | 27.20 (9.12) | 47.7 (8.98) |
| RL | 22.53 (7.96) | 53.61 (12.67) |
| EL | 26.07 (8.66) | 52.09 (12.20) |
| ELC | 58.77 (12.92) | 103.7 (16.10) |
| ADOS-2: | | |
| SA CSS | 8.55 (1.50) | - |
| RRB CSS | 8.59 (1.62) | - |
| Total CSS | 8.75 (1.51) | - |

Note. T scores ($M = 50$, $SD = 10$) were reported for the following MSEL scales: Visual Reception, (VR), Fine Motor (FM), Receptive Language (RL), and Expressive Language (EL). The Early Learning Composite (ELC) standard score ($M = 100$, $SD = 15$) was computed from these four scales and reflects general cognitive ability. TD children in our

sample scored significantly higher than children with ASD on the MSEL ELC ($t(61) = -12.158; p < .001, d = 3.083$). ADOS-2 Social Affect (SA) and Restricted, Repetitive Behavior (RRB), and Total Calibrated Severity Scores (CSS). Mean values are presented with standard deviation in parentheses.

Apparatus

Visual stimuli were displayed on a 17-inch LCD Tobii T120 eye-tracker via Tobii Studio's presentation software (Tobii Technology, Stockholm, Sweden). Sounds were played through external speakers centered behind the display. Participants were observed via a video camera on top of the screen and looking behavior during testing was monitored on Tobii Studio's Live Viewer. Eye movements were recorded at 60 Hz.

Stimuli

Search items were color-rendered photographs of an apple presented in a circular form ($5 \times 5^\circ$) and an oblong form ($2 \times 9^\circ$) (see Figure 1). The target was a real-world color/form combination (i.e., a red circular 'apple') and distractors were novel and opposite color/form combinations (i.e., a blue circular 'apple' and a red oblong 'apple'). The oddball item was always a red oblong 'apple' and appeared with a delayed onset (300 ms after search array onset). Search items were presented on a beige background with a 2° fixation cross and arranged inside a 23° diameter circle. The target was always present on each trial and located at a random distance from the central fixation. When the oddball was present it was always located in the same quadrant as the target.

Familiarization arrays (2 trials) consisted of the target and two regular distractors arranged in a triangular configuration. *Single-feature Search* arrays (5 trials) were single-feature search displays (color or shape) that consisted of the target and 8 distractors; either a set of red oblongs or a set of blue apples. Target detection in this context does not require effortful search and is highly efficient (Wolfe & Horowitz, 2004). Three single-feature trials were presented at the beginning of the experiment to highlight the special status of the target through ‘pop-out’ (Kaldy, Kraper, Carter, & Blaser, 2011; Treisman & Gelade, 1980). *Baseline Conjunction Search* arrays (6 trials) were feature-conjunction displays that consisted of the target and a set of distractors; red oblongs and blue apples. Target detection in this context requires effortful or inefficient search (Wolfe & Horowitz, 2004). Set size was 5, 9, and 13 items, in a quasi-random order. *Search with Oddball* arrays (6 trials) were identical to baseline conjunction search arrays however one of the red oblong distractors appeared 300 ms after the rest of the items in the search array. Set size was 5, 9, and 13 items, and varied quasi-randomly.

Procedure

Participants were seated on their caregiver’s lap, approximately 55–65 cm from the screen. Caregivers wore blacked-out sunglasses or kept their eyes closed, and were instructed not to talk to the child. Gaze was calibrated using a standard 5-point procedure (outer corners and center). Once a successful calibration was achieved, the visual search task commenced. At the beginning of each trial (except during the familiarization phase), the target moved into the center of the screen (~1 s) while a cartoon airplane sound effect

played. The target then jiggled (~1 s) while a honking sound effect played. The target then disappeared, and the search array appeared for 4 s (search period) accompanied by a tick-tock sound. Then, the target rotated back and forth for ~2 s accompanied by a cartoon applause sound effect (reward animation). During the familiarization phase the search array merely appeared for 4 s. The entire task lasted approximately 3 min 35 s.

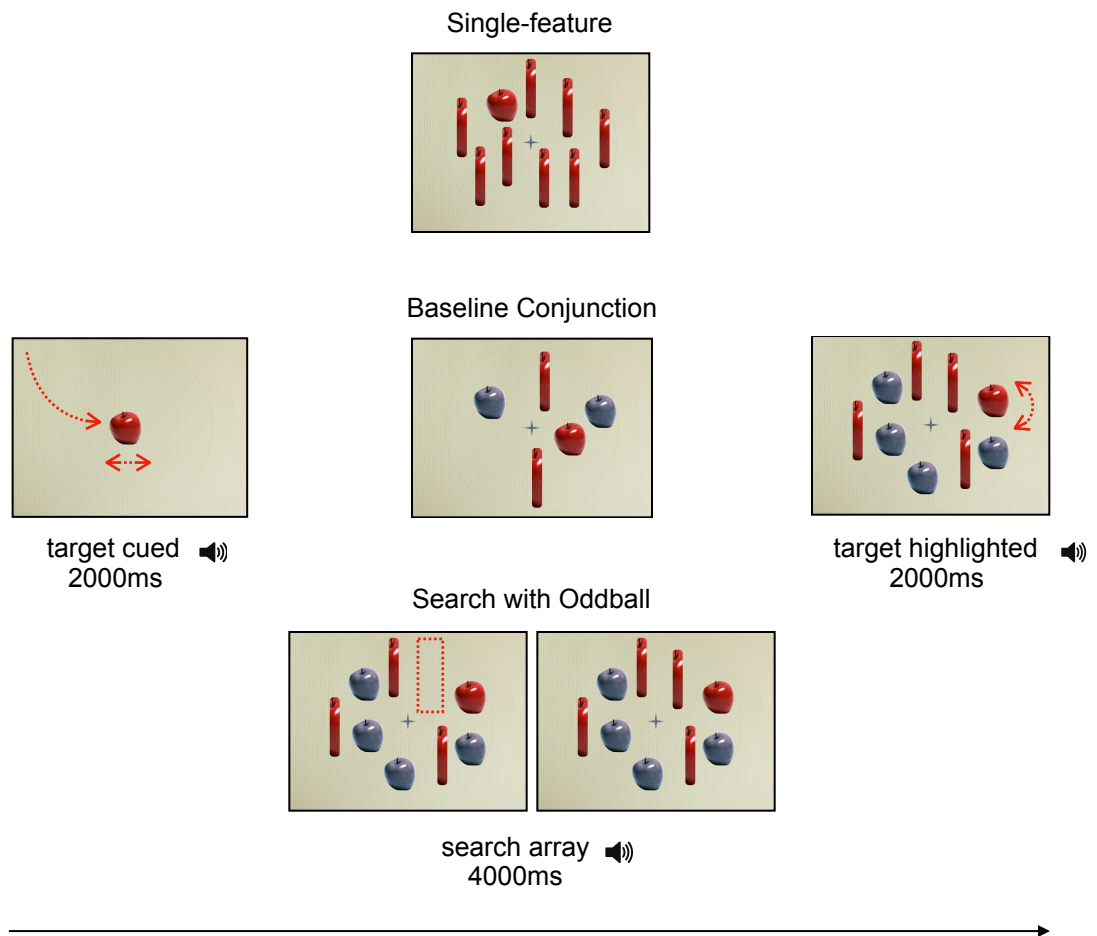


Figure 1. Experiment 1 trial structure and example stimuli. Novel onset oddball appeared 300 ms following search array onset.

Data analysis

Gaze positions were averaged between the two eyes to reduce noise. Fixations were defined using the Tobii I-VT filter, which classifies eye movements based on the velocity of the directional shifts of the eye (Olsen, 2012). Equal-sized areas of interest (AOIs) were defined for all search array items.

There were three main variables of interest: (1) hit rate, defined as the proportion of trials children fixated an item (target or oddball), (2) fixation duration (ms), defined as the total time children fixated an item (target, oddball, or a distractor²) in a trial, and (3) fixation latency (ms), defined as the total time elapsed between the first fixation to the screen and the first fixation to an item (target or oddball).

As children completed a small and variable number of trials, we used generalized estimating equations (GEE) to analyze search behavior (Jaeger, 2008). Statistical analyses were performed in SPSS 20. For repeated measurements, a compound symmetry covariance structure was assumed. Binary variables were analyzed using a binary logistic link function and continuous variables were analyzed using a linear link function.

Before conducting the main analyses, we ensured that data quality was comparable across the groups by filtering the data based on three criteria: (1) total number of eye-tracking samples recorded during the experiment needed to exceed 50% (participant level exclusion), (2) fixation latency to the screen needed to be less than 300 ms (trial level exclusion), and a minimum of one AOI needed to be fixated during the

² Median distraction fixation duration per trial was analyzed.

search period (trial level exclusion). We excluded trials where the latency to first fixate the screen exceeded 300 ms, to ensure participants were on screen at the time of the oddball onset. There was no significant difference in the number of valid trials retained between the ASD group and TD group (ASD: $M = 14.17$, $SD = 2.80$; TD: $M = 13.88$, $SD = 2.48$; $t(62) = 0.4301$, $p = .669$, $d = .105$). We also verified that task engagement was similar between the groups. There was no significant difference between the groups in the average fixation duration to the screen during the search periods ($\chi^2(1) = 1.580$, $p > .05$, ASD: $M = 3236$ ms, $SE = 55$ ms; TD: $M = 3127$ ms, $SE = 68$ ms).

Results

Attentional priority of target during baseline search

If children noted the special status of the target, they should attend to the target longer than a regular distractor. We compared target fixation duration on successful trials to the median distractor fixation duration during the baseline conjunction search phase (see Figure 3). This analysis revealed a significant main effect of Search Item ($\chi^2(1) = 41.258$, $p < .001$), demonstrating both of our groups of toddlers attended to the target longer than a regular distractor. There was no significant main effect of Diagnosis ($\chi^2(1) = .624$, $p > .05$) and no Diagnosis by Search Item interaction ($\chi^2(1) = .548$, $p > .05$).

Baseline search performance

Previous studies have found that individuals with ASD outperform TD individuals in visual search, leading to what has been termed the ‘visual search advantage’ in ASD (Kaldy et al., 2013). We used target hit rate as the primary measure of search

performance, as this measure has previously been shown to be sensitive to visual search differences in young children and when the search period is fixed (Gliga, Bedford, et al., 2015; Kaldy et al., 2011). In contrast to previous studies, we did not find a significant main effect of Diagnosis on target hit rate ($\chi^2(1) = .004, p > .05$, ASD: $M = 74\%$, $SE = 5.1\%$; TD: $M = 74\%$, $SE = 4.3\%$) (see Figure 2). As another measure of search efficiency, we analyzed fixation latency to the target (this measure is more similar to reaction time used in adult studies of visual search). There was no significant main effect of Diagnosis on target fixation latency ($\chi^2(1) = .077, p > .05$, ASD: $M = 1614$ ms, $SE = 117$ ms; TD: $M = 1651$ ms, $SE = 67$ ms) (see Figure 4).

Attentional priority of novel onset oddball

If toddlers with ASD show reduced sensitivity to novel onset stimuli, they should demonstrate reduced attention to the novel onset oddball in our task. An analysis of oddball hit rate revealed no main effect of Diagnosis, suggesting detection rates were similar between toddlers with ASD and toddlers with TD ($\chi^2(1) = 1.723, p > .05$, ASD: $M = 78\%$, $SE = 3.6\%$; TD: $M = 71\%$, $SE = 4.0\%$) (see Figure 2). We then compared oddball fixation latency to target fixation latency to determine if the novel onset oddball was fixated, on average, faster than the target, and, if the groups differed in how they prioritized either item (see Figure 4). We did not observe a main effect of Diagnosis ($\chi^2(1) = 2.052, p > .05$). However, our analysis revealed a significant main effect of Search Item ($\chi^2(1) = 40.548, p < .001$): children were overall faster orienting to the oddball compared to the target. Critically, this effect was not qualified by an interaction with

Diagnosis ($\chi^2(1) = .212, p > .05$): toddlers with and without ASD showed equally strong orienting biases to the novel onset oddball. Lastly we compared fixation duration to the oddball to median distractor fixation durations (see Figure 3).

If, once fixated, the oddball was attended longer than a regular distractor, this would indicate that the oddball was effective at capturing attention. This analysis revealed a significant main effect of Item type ($\chi^2(1) = 38.966, p < .001$): children looked longer at the oddball compared to a regular distractor. However, there was no main effect of Diagnosis ($\chi^2(1) = 1.198, p > .05$), and no significant Item by Diagnosis interaction ($\chi^2(1) = .233, p > .05$), demonstrating fixation durations to the oddball were comparable between our two groups.

Effect of novel onset oddball on visual search

As the novel onset oddball was both salient and task-irrelevant, we asked whether attending to this item affected visual search performance. First we compared target hit rate at Baseline to target hit rate in the presence of the oddball (see Figure 2). This analysis revealed no significant main effect of Diagnosis ($\chi^2(1) = .012, p > .05$), and a significant main effect of Search Phase ($\chi^2(1) = 4.866, p = .027$). The interaction was not significant ($\chi^2(1) = .025, p > .05$). Both toddlers with ASD and TD toddlers demonstrated a significant decrease in target hit rates when the oddball was present. To clarify whether this effect was driven by the oddball (as opposed to general fatigue with the task over time), we asked whether the target hit rate was affected by the oddball hit rate (see Figure 5). We entered target hit rate as the dependent variable, and as the

independent variables we entered Diagnosis, Oddball Hit Rate (i.e., hit or miss), and their interaction. This analysis yielded a marginally significant main effect of Oddball Hit Rate ($\chi^2(1) = 3.686, p = .055$), suggesting that noticing the oddball may have facilitated target detection, and vice versa. Importantly, there was no main effect of Diagnosis ($\chi^2(1) = .603, p > .05$) and no Diagnosis by Oddball Hit Rate interaction ($\chi^2(1) = .357, p > .05$), indicating that the effect of the oddball on visual search was comparable between our two groups.

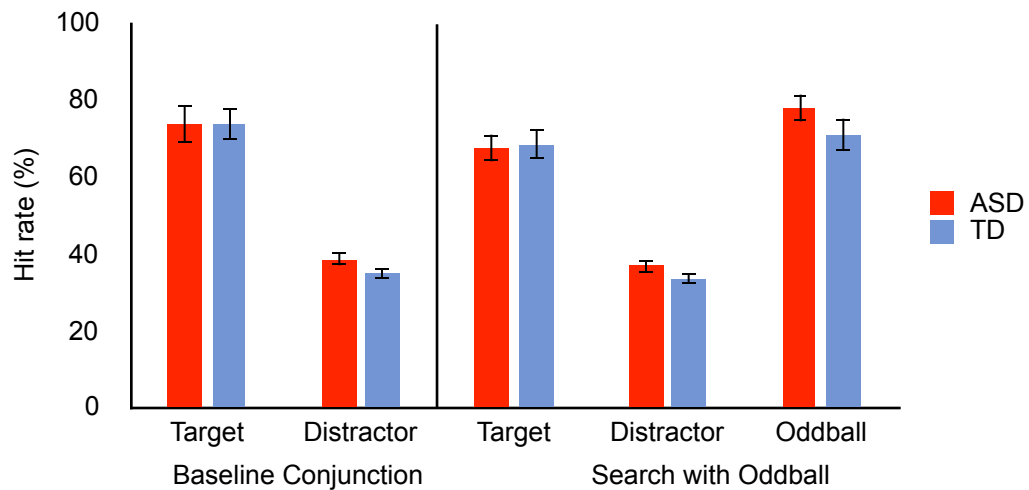


Figure 2. Experiment 1 hit rates (%). Distractor hit rate is plotted for reference (number of distractors fixated divided by total number of distractors present, averaged). Bars are 1 standard error.

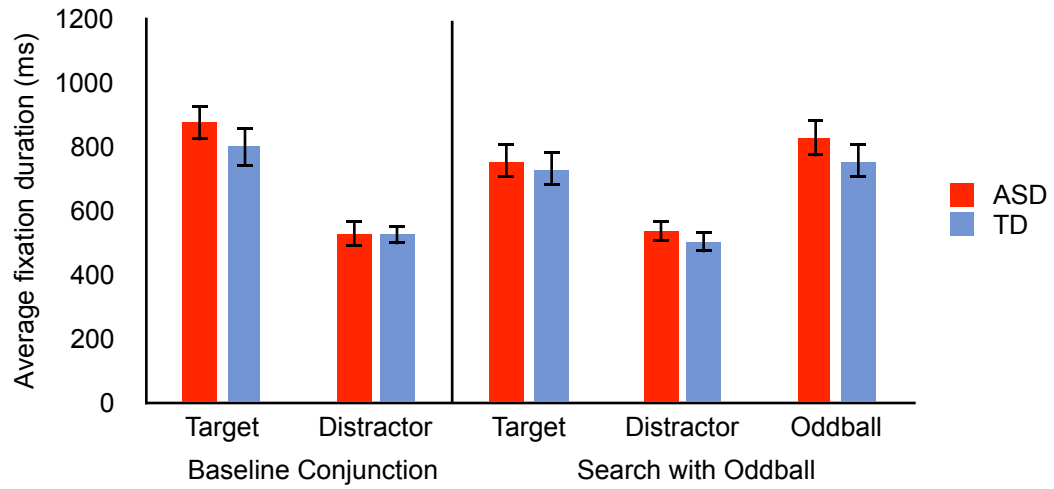


Figure 3. Experiment 1 average fixation durations (ms). Bars are 1 standard error.

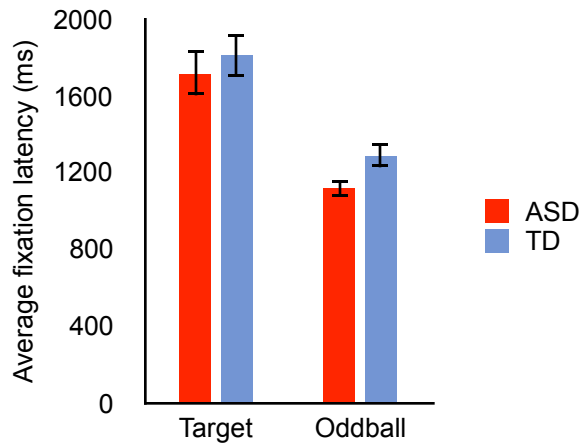


Figure 4. Experiment 1 average fixation latencies (ms) during the search with oddball phase. Bars are 1 standard error.

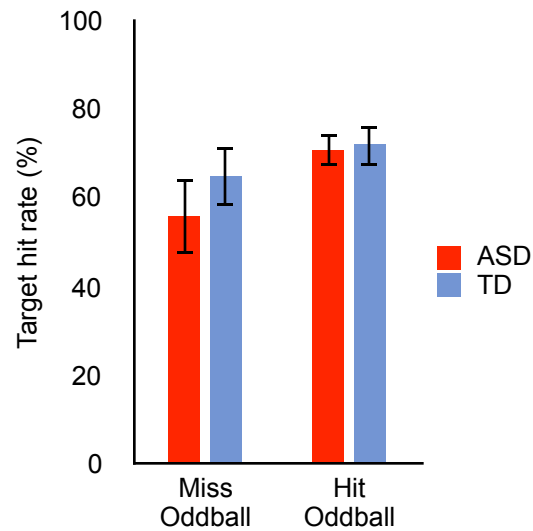


Figure 5. Experiment 1 target hit rate (%) by oddball hit rate during the search with oddball phase. Bars are 1 standard error.

Discussion

Here we examined how the introduction of a novel onset oddball during conjunction visual search affects attention allocation in toddlers just diagnosed with ASD and TD chronologically age-matched controls. Children with and without ASD were equally fast to orient to the novel onset oddball, and did so faster than the target. Further, the novel onset oddball captured attention to a similar extent for both groups: oddball hit rate was not different between toddlers with ASD and TD toddlers, and both groups fixated the oddball longer than a regular distractor, with no differences between the groups in the magnitude of this attentional capture. Thus, we found no evidence of

atypical allocation of attention to a novel task-irrelevant onset oddball in young toddlers with ASD.

Our finding of typical allocation to novel onset stimuli was unexpected, given previous studies conducted with older children and adults (e.g., Greenaway & Plaisted, 2005; Keehn & Joseph, 2008). It is unclear why toddlers with ASD performed typically in our task. Given previous studies have been conducted with older children, it is possible atypicalities in the allocation of attention to dynamic stimuli emerge later in development. However, there are also several methodological differences between our study and the previous studies, making it difficult to determine what factors underlie typical performance in our study.

Given the novel onset oddball in our task was both salient and task-irrelevant, we considered how attending to this item affected visual search. First and foremost, target hit rate was reduced in the presence of the oddball, suggesting the oddball impaired visual search in both of our groups. In our task, finding the oddball was associated with a greater likelihood of finding the target. As the target and the oddball were always located in the same quadrant, it is possible that orienting to this item facilitated target orienting and vice versa. Regardless, this effect was not dependent on diagnosis. Thus, attention to the novel onset oddball was not altered in children with ASD between 17 and 36 months of age.

Experiment 2

As discussed previously, there is evidence that selective attention in ASD may demonstrate stimulus-specific atypicalities. However, in Experiment 1, we did not observe reduced sensitivity to novel onsets in toddlers just diagnosed with ASD relative to TD controls. In Experiment 2, we examined how the introduction of a novel colored oddball during visual search affects attention allocation in toddlers just diagnosed with ASD and TD age-matched controls. As in Experiment 1, in Experiment 2, toddlers were tasked with searching for a red apple target among feature-conjunction distractors (blue apples and red oblong shapes) and after a series of baseline trials, a novel oddball was introduced into the search array. However, in Experiment 2, the oddball was a novel color (either orange or green, see Figure 6).

Methods

Participants

Children with TD were recruited from the Greater Boston area via mailings. Children diagnosed with ASD were recruited through local early intervention agencies and participation occurred at the beginning of the visit in which diagnostic testing was later performed. Following the experimental procedure, the general cognitive functioning of all children was assessed using the Mullen Scales of Early Learning (MSEL; Mullen & others, 1995).

For children with ASD, clinical diagnosis was assigned by a licensed psychologist using the Autism Diagnostic Observation Schedule-2 (Lord, Rutter, et al., 2012; Lord,

Luyster, Gotham, & Guthrie, 2012) (Toddler Module, $N = 21$; Module 1, $N = 13$). Calibrated severity scores (CSS) were calculated using the method described by Esler et al. (2015) (Toddler Module) and Hus et al. (2014) (Module 1 and 2). For children with TD, we verified that no participant had a history of neurological disorders, developmental issues, ASD behaviors, or siblings with developmental disorders via parental report. Typical development was determined using the Early Learning Composite standard score (ELC) on the MSEL and scores on the Brief Infant–Toddler Social and Emotional Assessment (BITSEA) (Briggs-Gowan et al., 2004). An ELC on the MSEL below 70 is 2 SD below the standardized mean and equivalent to a “well below average” level of cognitive development. Children who did not meet criteria for TD (2 children) or for ASD (4 children) were excluded. Participants had no known vision impairments or first-degree relatives with colorblindness.

Forty-five children with TD and forty children diagnosed with ASD were tested. Fifteen of these children were excluded because of poor eye-track quality (5 TD, 5 ASD) or for not meeting the minimum valid trial criterion (4 TD, 1 ASD; see Data Analysis). The final participant sample was 36 children with TD and 34 children diagnosed with ASD. Participants’ were chronologically age matched (TD: $M = 28.12$, $SD = 4.81$; ASD: $M = 25.57$, $SD = 5.46$). Table 2 shows a summary of participants’ demographic information and assessment scores.

Table 2. Summary of participants' demographic information and scores on standardized assessments in Experiment 2.

| | ASD | TD |
|------------------------|---------------|----------------|
| N | 34 | 36 |
| # Females | 7 | 16 |
| Age (months) | 25.57 (5.46) | 28.12 (4.81) |
| range | 14.54 - 33.88 | 18.62 - 36.51 |
| Valid trials collected | 14.17 (2.80) | 13.88 (2.48) |
| Ethnicity (# children) | | |
| Hispanic or Latino | 19 | 7 |
| Not Hispanic or Latino | 10 | 28 |
| Not reported | 5 | 1 |
| Mullen Scales: | | |
| VR | 35.35 (10.63) | 61.58 (9.34) |
| FM | 32.82 (9.10) | 50.13 (8.59) |
| RL | 22.56 (6.68) | 56.35 (9.59) |
| EL | 29.26 (8.75) | 55.42 (11.85) |
| ELC | 63.91 (9.88) | 111.74 (15.32) |
| ADOS-2: | | |
| SA CSS | 9.29 (1.19) | - |
| RRB CSS | 8.1 (1.34) | - |
| Total CSS | 7.83 (2.07) | - |

Note. T scores ($M = 50$, $SD = 10$) were reported for the following MSEL scales: Visual Reception, (VR), Fine Motor (FM), Receptive Language (RL), and Expressive Language (EL). The Early Learning Composite (ELC) standard score ($M = 100$, $SD = 15$) was

computed from these four scales and reflects general cognitive ability. TD children in our sample scored significantly higher than children with ASD on the MSEL ELC ($t(63) = -15.092; p < .001, d = 3.71$). ADOS-2 Social Affect (SA), Restricted, Repetitive Behavior (RRB), and Total (Total) Calibrated Severity Scores (CSS) were measured for children diagnosed with ASD. Mean values are presented with standard deviation in parentheses.

Apparatus & Stimuli

Apparatus and stimuli were identical to Experiment 1 with the following exception: the oddball item was always an orange or green oblong (see Figure 6).

Procedure

The procedure was similar to Experiment 1. At the beginning of each trial (except during the Familiarization phase), the target moved into the center of the screen (~1 s) while a cartoon airplane sound effect played. The target then disappeared, and the search array appeared for 4 s (search period) accompanied by a tick-tock sound. Then, the target rotated back and forth for ~2 s accompanied by a cartoon applause sound effect (reward animation). During the Familiarization phase the search array merely appeared for 4 s. The entire task lasted approximately 3 min 35 s.

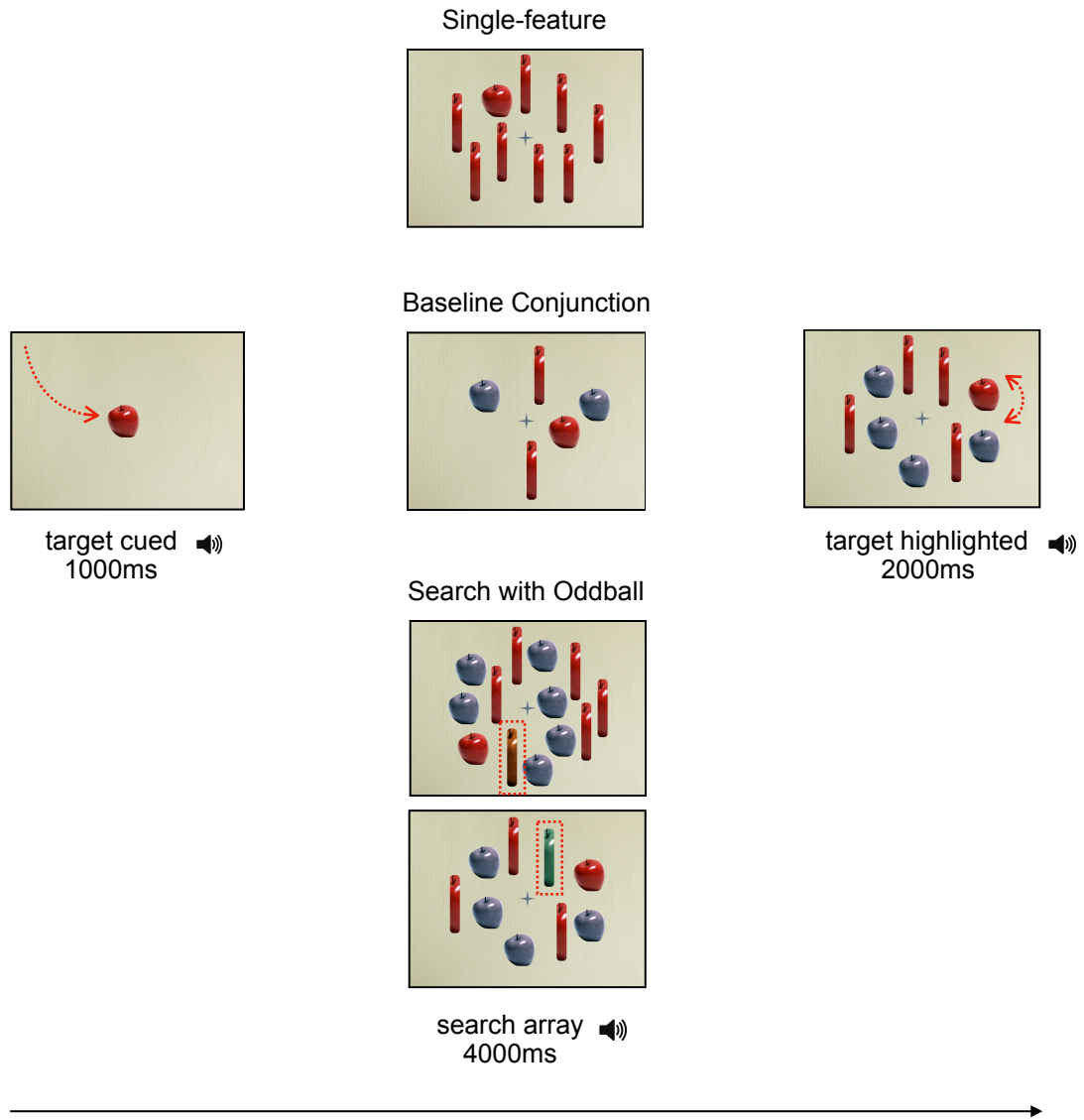


Figure 6. Experiment 2 trial structure and example stimuli.

Data analysis

Gaze positions were averaged between the two eyes to reduce noise. Fixations were defined using the Tobii I-VT filter, which classifies eye movements based on the

velocity of the directional shifts of the eye (Olsen, 2012). Equal-sized areas of interest (AOIs) were defined for all search array items.

There were three main variables of interest: (1) hit rate, defined as the proportion of trials children fixated an item (target or oddball), (2) fixation duration (ms), defined as the total time children fixated an item (target, oddball, or a distractor³) in a trial, and (3) fixation latency (ms), defined as the total time elapsed between the first fixation to the screen and the first fixation to an item (target or oddball).

As children completed a small and variable number of trials, we used generalized estimating equations (GEE) to analyze search behavior (Jaeger, 2008). Statistical analyses were performed in SPSS 20. For repeated measurements, a compound symmetry covariance structure was assumed. Binary variables were analyzed using a binary logistic link function and continuous variables were analyzed using a linear link function. Before conducting the main analyses, we ensured that data quality was comparable across the groups by filtering the data based on three criteria: (1) total number of eye-tracking samples recorded during the experiment needed to exceed 50% (participant level exclusion), (2) fixation latency to the screen needed to be less than 300 ms (trial level exclusion) to facilitate comparison with Experiment 1, and a minimum of one AOI needed to be fixated during the search period (trial level exclusion). This resulted in more valid trials being retained for the ASD group than the TD group (ASD: $M = 14.71$, $SD = 2.80$; TD: $M = 13.03$, $SD = 2.91$; $t(68) = 2.399$, $p = .009$, $d = .573$). Importantly, task

³ Median distraction fixation duration per trial was analyzed.

engagement was similar between the groups: there was no significant difference between the groups in fixation duration to the screen during the search period ($\chi^2(1) = .684, p > .05$, ASD: $M = 3181$ ms, $SE = 83$ ms; TD: $M = 3269$ ms, $SE = 55$ ms).

Results

Attentional priority of target during baseline search

If children noted the special status of the target, they should attend to the target longer than a regular distractor. We compared target fixation duration on successful trials to the median distraction fixation duration on each trial during the baseline conjunction search phase (see Figure 8). This analysis revealed a significant main effect of Search Item ($\chi^2(1) = 73.902, p < .001$), demonstrating both of our groups of toddlers attended to the target longer than a regular distractor. There was no significant main effect of Diagnosis ($\chi^2(1) = 2.252, p > .05$) and no Diagnosis by Search Item interaction ($\chi^2(1) = 2.958, p > .05$).

Baseline search performance

As in Experiment 1, we did not find a significant main effect of Diagnosis on target hit rate ($\chi^2(1) = .024, p > .05$, ASD: $M = 75\%$, $SE = 4.3\%$; TD: $M = 75\%$, $SE = 3.4\%$) (see Figure 7). We also analyzed fixation latency to the target. There was no significant main effect of Diagnosis on target fixation latency ($\chi^2(1) = .381, p > .05$, ASD: $M = 1482$ ms, $SE = 92$ ms; TD: $M = 1402$ ms, $SE = 91$ ms).

Attentional priority of novel colored oddball

If toddlers with ASD show reduced sensitivity to novel color stimuli, they should demonstrate reduced attention to the novel color oddball in our task. An analysis of oddball hit rate revealed no main effect of Diagnosis, suggesting detection rates were similar between toddlers with ASD and toddlers with TD ($\chi^2(1) = 3.053, p > .05$, ASD: $M = 53\%$, $SE = 3.8\%$; TD: $M = 64\%$, $SE = 4.8\%$) (see Figure 7). We then compared oddball fixation latency to target fixation latency to determine if the novel onset oddball was fixated, on average, faster than the target, and, if the groups differed in how they prioritized either item (see Figure 9). This analysis revealed a no main effect of Search Item ($\chi^2(1) = .250, p < .05$), illustrating that overall time to find the novel colored oddball was similar to the target. We did not observe a main effect of Diagnosis ($\chi^2(1) = 2.325, p > .05$) or an interaction with Diagnosis ($\chi^2(1) = 2.373, p > .05$): toddlers with and without ASD showed equally strong orienting biases to the novel colored oddball. Lastly, we compared fixation duration to the oddball to median distractor fixation durations (see Figure 8). If once fixated, the oddball was attended longer than a regular distractor, this would indicate that the oddball was effective at capturing attention. This analysis revealed a significant main effect of Item type ($\chi^2(1) = 65.171, p < .001$), illustrating longer fixation durations to the novel colored oddball compared to a regular distractor. Importantly, we observed a main effect of Diagnosis ($\chi^2(1) = 6.233, p = .013$), which was qualified by a significant Diagnosis by Item type interaction ($\chi^2(1) = 12.944, p < .001$). Post hoc comparisons indicated average fixation durations to the novel colored oddball

were longer than a distractor for both toddlers with ASD ($p < .001$, $d = .834$) and TD toddlers ($p < .001$, $d = 1.592$), however toddlers with ASD showed shorter fixation durations to the oddball relative to TD toddlers ($p = .001$, $d = .776$).

Effect of novel colored oddball on visual search

As the novel colored oddball was both salient and task-irrelevant, we asked whether attending to this item affected visual search performance. First, we compared target hit rate at Baseline to target hit rate in the presence of the oddball (see Figure 7). This analysis revealed no significant main effect of Diagnosis ($\chi^2(1) = .336$, $p > .05$), no main effect of Search Phase ($\chi^2(1) = 3.316$, $p > .05$), and no Diagnosis by Search Phase interaction ($\chi^2(1) = 1.315$, $p > .05$). Neither toddlers with ASD or TD toddlers demonstrated a change in target hit rate when the oddball was present. We also asked whether the target was less likely to be fixated on trials where the oddball was also fixated (see Figure 10). We entered target hit rate as the dependent variable, and as the independent variables, we entered Diagnosis, Oddball Hit Rate (i.e., hit or miss), and their interaction. This analysis yielded a significant main effect of Oddball Hit Rate ($\chi^2(1) = 4.717$, $p = .03$), suggesting that orienting to the oddball facilitated target detection, and vice versa. Importantly, there was no main effect of Diagnosis ($\chi^2(1) = 1.565$, $p > .05$) and no Diagnosis by Oddball Hit Rate interaction ($\chi^2(1) = .204$, $p > .05$), indicating that the effect of the oddball on visual search was comparable between our two groups. An exploratory analysis of the proportion of the different outcomes has shown that the proportion of trials where participants only managed to find one of the two special items

(target or oddball) was approximately equal between the two groups (42.1 vs. 42.8%) (see Figure 11). A Fisher's exact test on the number of trials where children only found the Oddball vs. the Target showed a significant Group difference ($p = .018$, two-tailed). When they only managed to find one of the two special items within the search period, in the ASD group this item was more likely to be the target than in TD controls.

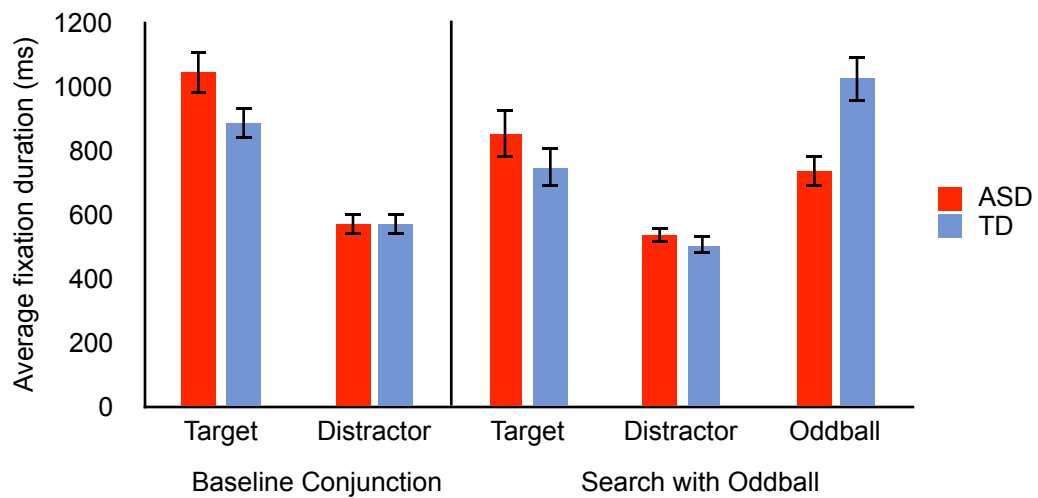


Figure 7. Experiment 2 hit rates (%). Distractor hit rate is plotted for reference (number of distractors fixated divided by total number of distractors present, averaged). Bars are 1 standard error.

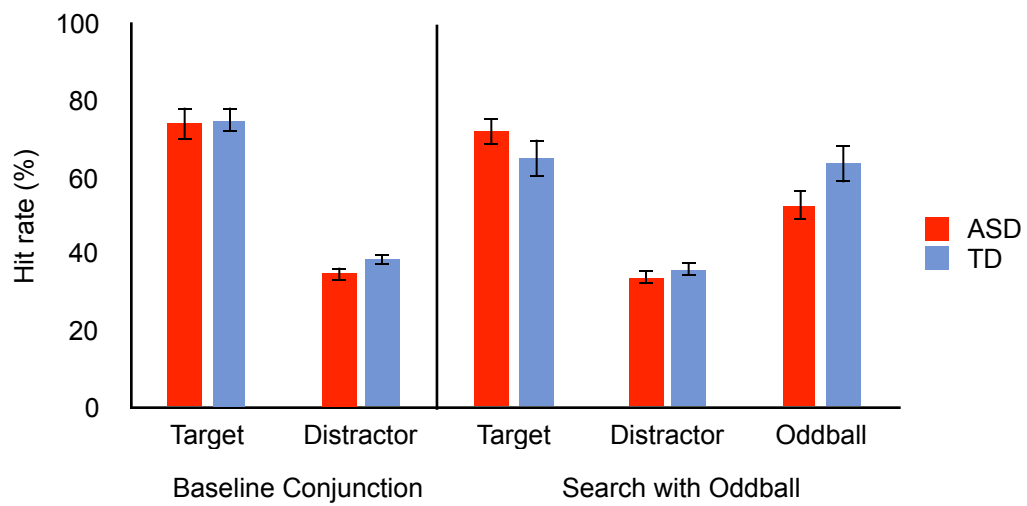


Figure 8. Experiment 2 average fixation durations (ms). Bars are 1 standard error.

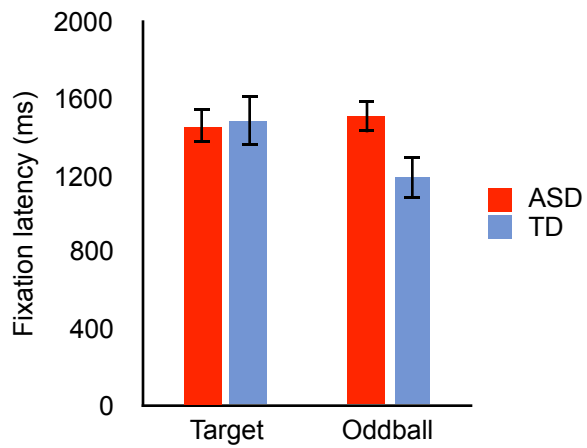


Figure 9. Experiment 2 average fixation latencies (ms) during the search with oddball phase. Bars are 1 standard error.

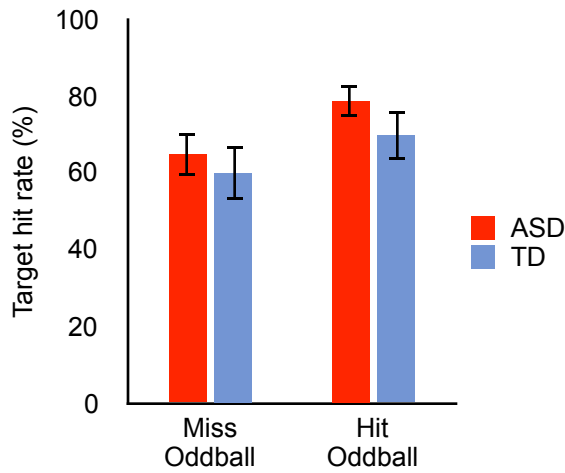


Figure 10. Experiment 2 target hit rate (%) by oddball hit rate during the search with oddball phase. Bars are 1 standard error.

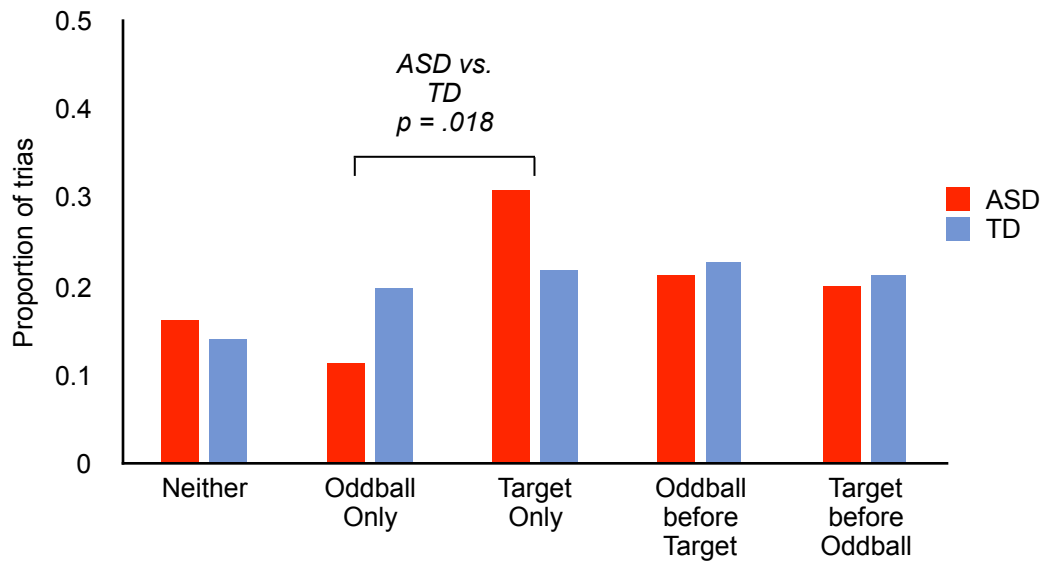


Figure 11. Experiment 2 breakdown of hits and misses per trial during the search with oddball phase. Proportion of trials is plotted.

Effect of participant characteristics on attentional priority of the novel colored oddball

Our analyses revealed that toddlers with ASD showed reduced fixation durations to the novel colored oddball item relative to TD toddlers. We therefore asked whether fixation duration to the oddball item was related to ASD clinical symptoms in the ASD group. Spearman's correlations between the average oddball fixation duration and ADOS Social Affect, Restricted Repetitive Behavior, and Total CSS revealed no statistical relationships ($\rho < 0.76, p > 0.675$). Our two groups were not matched for Mullen scores, which were significantly lower in our group of toddlers with ASD. We therefore asked whether fixation duration to the oddball item was related to general intellectual ability in either group. For the ASD group, average oddball fixation duration was positively related to Visual Reception score ($\rho = .386, p = .027$), Fine Motor score ($\rho = .357, p = .041$), Expressive Language score ($\rho = .415, p = .016$), and Early Learning Composite Standard score ($\rho = .490, p = .004$). This effect was not driven by generally longer fixations — there was no statistical relationship between the above participant variables and average target fixation duration ($\rho < 0.256, p > 0.145$). In the TD group, no correlations were found between average oddball fixation duration and Mullen scores ($\rho < .276, p > .164$). The group difference between the correlation coefficients was not statistically significant ($ps > .129$, one-tailed). Chronological age (in months) was not related to average oddball fixation duration in either the ASD ($\rho = -.233, p = .191$) or TD group ($\rho = .155, p = .398$). See Figure 12.

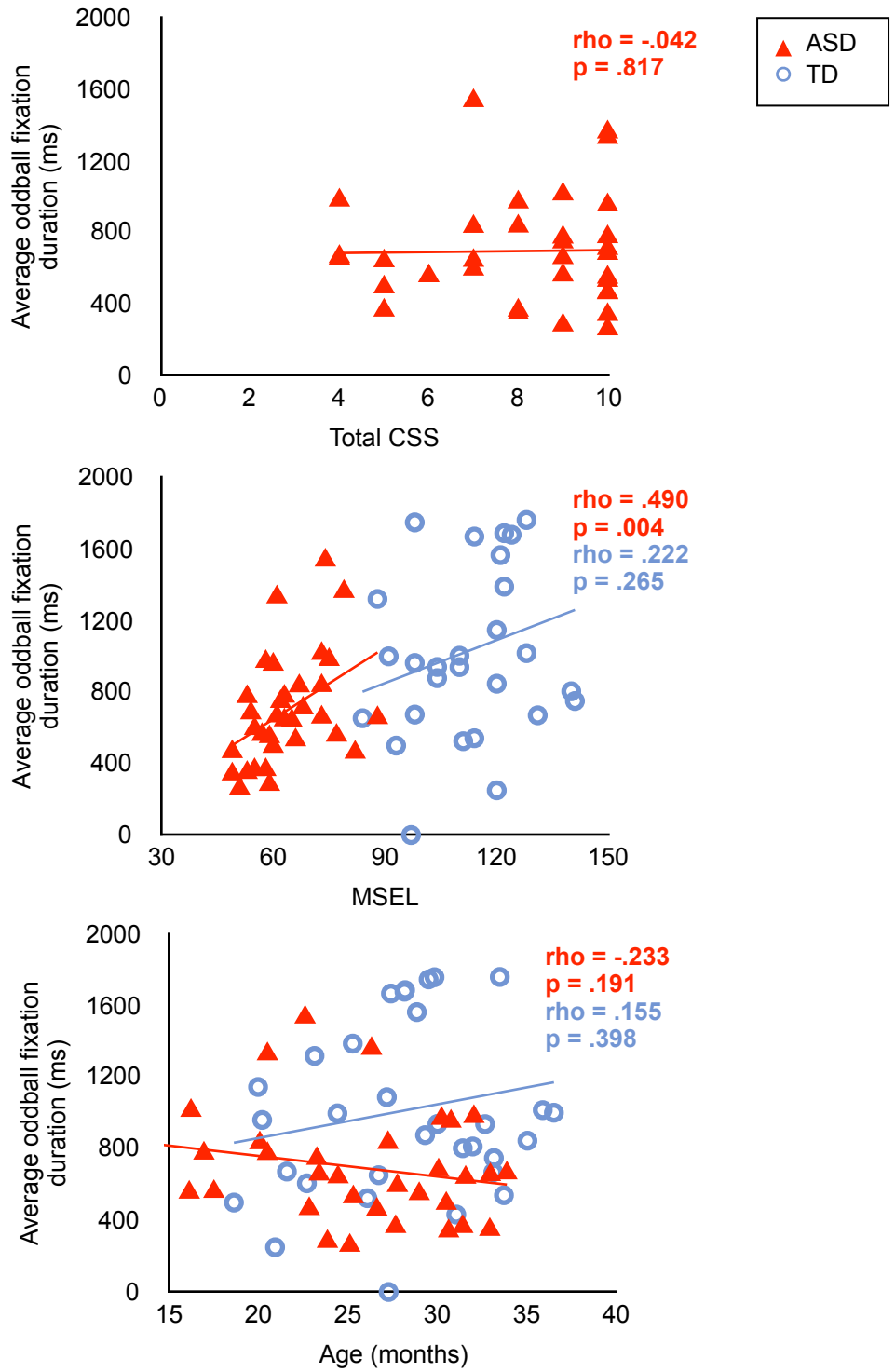


Figure 12. Relations between participant characteristics and attentional priority of the novel colored oddball in Experiment 2.

Discussion

Here we investigated whether attention to task-irrelevant novel stimuli depended on specific stimulus properties — toddlers were tasked with searching for a conjunction target in the presence of a task-irrelevant novel colored oddball. Both groups of toddlers detected the novel colored oddball and attended to it longer than a regular distractor, indicating the oddball was effective at capturing attention. However, toddlers with ASD demonstrated significantly reduced fixation durations to the colored oddball relative to TD toddlers. Thus, while the oddball appeared to modulate attention in toddlers with ASD, it did so to a lesser extent than TD toddlers. It is important to note that oddball hit rate was not different between toddlers with ASD and TD toddlers, and so detection of novel colored stimuli does not appear to be impaired. Target hit rate was similar during the Oddball phase and the Baseline phase, suggesting the oddball did not impair visual search. This finding is in contrast to Experiment 1, where search was found to be impaired in the presence of the oddball. Yet, as in Experiment 1, attentional capture by the oddball may have facilitated search, canceling out any detrimental effect on visual search performance: finding the oddball was associated with a greater likelihood of finding the target. This effect was not dependent on Diagnosis, however.

To evaluate whether atypicalities in processing task-irrelevant novel stimuli are linked to core ASD symptoms, we examined associations between attention to the novel colored oddball and behavioral observational measures of ASD-related symptoms in Experiment 2. Evidence linking a specific attentional impairment to the core social-

communicative symptoms would lend support to theories suggesting attentional modulation atypicalities are not merely associated or secondary features of ASD but are of deeper etiological significance with regard to the defining symptoms of ASD and their neurobiological underpinnings. However, ASD clinical symptoms were not related to increased attention to the oddball. Interestingly, there were positive relationships between multiple measures of intellectual ability (Visual Reception, Fine Motor, Expressive Language, and Early Learning Composite Score) that was not present in the TD group, suggesting developmental level may moderate attentional capture in children with ASD.

General Discussion

In two experiments we examined attention to a task-irrelevant novel oddball during visual search. Our findings suggest that attention to task-irrelevant novel stimuli depends on stimulus properties and that toddlers with ASD have a particular deficit in attentional modulation by salient colored stimuli.

The results from the present studies are most in line with the claim that selective attention in toddlers with ASD is overly selective, narrow, or over-focused (Behrmann, Thomas, & Humphreys, 2006; Happe & Frith, 2006; Robertson, et al., 2013). However this aspect of attention in ASD appears to depend on stimulus properties, and specifically there appears to be an impairment in attentional modulation by color.

Atypical development of attention in ASD has increasingly been recognized as an important area for research: early differences in attention precede core diagnostic symptoms and are among the earliest indicators of risk for ASD (Elison et al., 2013;

Elsabbagh et al., 2013a; Zwaigenbaum et al., 2005a). Current accounts of selective attention in young children with ASD have been informed primarily by tasks that measure exogenous control in passive viewing contexts. Here the claim has been that attention is ‘sticky’, despite mixed evidence (Elison et al., 2012; Gliga, Smith, et al., 2015; Sacrey et al., 2014). In our study, we did not observe any evidence that children with ASD explored the search array differently from TD children. Median fixation duration to a regular distractor was not significantly longer for toddlers with ASD relative to TD toddlers.

Selective attention in the real world requires focusing attentional resources on relevant information while ignoring irrelevant information. Furthermore, the typical development of attention during early childhood marks a transition from primarily exogenous forms of control to endogenous forms of control. In TD individuals less robust endogenous control of attention during early childhood may increase distractibility, however it may also be adaptive, ensuring young children do not miss potentially important opportunities for learning about the world (Plebanek & Sloutsky, 2017; Tighe, Glick, & Cole, 1971). Our findings suggest that endogenous control may be overly robust in young toddlers with ASD, leading to reduced exploration of novel task-irrelevant information.

Finally, in contrast to previous visual search studies conducted with children (Gliga, Bedford, et al., 2015; Kaldy et al., 2011; Plaisted et al., 1998) toddlers with ASD did not outperform TD toddlers in our task. While we did not observe a visual search

advantage, toddlers with ASD were not impaired relative to chronologically age-matched TD controls, demonstrating that visual search is an area of strength for children with ASD (Burack et al., 2016).

CHAPTER 3

SPECIFIC AIM 2: ATTENTIONAL SET-SHIFTING IN TODDLERS WITH AND WITHOUT ASD

Executive control is a set of related, higher-order cognitive skills that enable an individual to shift from one mental set to another (set-shifting), suppress a dominant response (inhibitory control), and actively maintain and manipulate information in mind (working memory) (Diamond, 2013; Garon et al., 2008; Miyake et al., 2000). Executive control is considered essential for voluntary and flexible control of thoughts and behavior, and robust executive control in childhood is predictive of a range of positive cognitive and socio-emotional outcomes later in life (Diamond, 2013).

There has long been an interest in the link between impaired executive control and behavioral inflexibility in ASD. Individuals with ASD often get “stuck” on an idea or action, have difficulty with perspective taking, and show distress or oppositional behavior when faced with change — a symptom profile that could easily be explained by a primary deficit in executive control. As such, the executive control hypothesis has been

highly influential in neurocognitive theories of ASD (Hill, 2004; Hughes, Russell, & Robbins, 1994; Ozonoff, Pennington, & Rogers, 1991; Pennington & Ozonoff, 1996).

Substantial empirical support for the executive control hypothesis in ASD has come from assessments of set-shifting in older children and adults with ASD (for reviews, see Demetriou et al., 2017; Geurts, Corbett, & Solomon, 2009; Leung & Zakzanis, 2014). Set-shifting tasks are widely used as measures of executive control and involve two phases: (1) an initial training phase where the participant learns a rule (or adopts a ‘mental set’), and (2) a switch phase, where the participant is tasked with switching to a new rule that conflicts with the initial rule. On standard set-shifting tasks, such as the Wisconsin Card Sort Task (R. K. Heaton, Chelune, Talley, Kay, & Curtiss, 1993), older children and adults with ASD are more likely than typically developing controls to continue to implement the initial rule rather than the new rule (perseverative responding), and/or switch to the new rule then regress to the initial rule (failure to maintain set) (Landry & Al-Taie, 2016).

While an executive control impairment appears to be well-established in older children and adults with ASD, only a handful of studies have examined performance on set-shifting tasks in children with ASD younger than 5 years of age. This is surprising given that problems with behavioral flexibility are well-established in young children diagnosed with ASD, and high levels of repetitive behavior during infancy is predictive of an ASD diagnosis in children at high familial risk for ASD (Elison et al., 2014; Leekam, Prior, & Uljarevic, 2011).

In TD individuals, executive control emerges progressively during early childhood, with simpler executive control skills emerging prior to more complex ones (Best & Miller, 2010; Garon et al., 2008; Zelazo, 2004). For example, by the end of the first year of life, infants can successfully maintain a representation of a hidden toy in mind and inhibit a tendency to search for that object at previous hiding location (Diamond & Goldman-Rakic, 1989). During the preschool period, children become increasingly able to hold conflicting rules in mind and flexibly shift attention between those rules (Garon et al., 2008; Hendry et al., 2016). For example, on standard versions of the Dimensional Change Card Sort (DCCS) (Frye et al., 1995) most children aged 3 show difficulty switching to a new rule that conflicts with the initially learned rule (or ‘mental set’), while most children aged 4-5 switch rules with ease (for a review, see Doebel & Zelazo, 2015).

Currently, it is unclear how set-shifting develops in young children with ASD. Studies employing complex attentional set-shifting paradigms (such as the DCCS) in preschool-aged children diagnosed with ASD suggest that the development of executive control in this population might be delayed: preschoolers with ASD make more perseverative errors and take longer to reach criterion following a switch compared to chronologically age-matched TD controls (Garon et al., 2017; Kimhi, Shoam-Kugelmas, Ben-Artzi, Ben-Moshe, & Bauminger-Zviely, 2014; Pellicano et al., 2017; Pellicano, Maybery, Durkin, & Maley, 2006) and mental age-matched TD controls (McEvoy, Rogers, & Pennington, 1993). On the other hand, studies employing simpler response

shifting paradigms (such as the A-not-B task, Piaget, 1954; or the Spatial Reversal task, Kaufman, Leckman, & Ort, 1989) suggest deficits in executive control are not a primary factor in the development of behavioral inflexibility in young children diagnosed with ASD: preschoolers with ASD performed equivalently to chronologically age-matched TD controls (Dawson et al., 2002; Griffith, Pennington, Wehner, & Rogers, 1999; Yerys, Hepburn, Pennington, & Rogers, 2007).

To examine attentional set-shifting in young toddlers just-diagnosed with ASD, we developed a novel set-shifting paradigm that combines visual search with eye-tracking. We assessed toddlers with ASD and chronologically age-matched TD controls (age range: 15-37-months). This age range is both the earliest at which an ASD diagnosis can be made, and the period where even the typical development of attentional set-shifting has been understudied (but see Blakey, Visser, & Carroll, 2016). Toddlers were tasked with searching for one of two potential targets presented among a set of feature-conjunction distractors. We compared performance prior to and following a target switch — after a fixed set of trials, the currently *relevant* target became *irrelevant* and the currently *irrelevant* target became *relevant*. In TD adults, a switch in search target leads to ‘switch cost’ — slower reaction times and increased errors (e.g. Fox, 1995; Maljkovic & Nakayama, 1994; Tipper, 1985; Wolfe et al., 2003; Vickery, King, & Jiang, 2005). Rather than a manual or a verbal response, we measured attentional set-shifting via gaze behavior (Chevalier, Dauvier, & Blaye, 2017; Wass, Porayska-Pomsta, & Johnson, 2011). Unlike traditional attentional set-shifting paradigms, our paradigm ensures that the ASD

group is not at a relative disadvantage: (1) it uses visual search, a skill that is well-documented to be equal or superior in children with ASD compared to age-matched controls (Kaldy et al., 2013), (2) it does not require verbal instructions or verbal responses, reducing the relevance of verbal fluency on task performance.

Experiment 3

Methods

Participants

We calculated the minimum required sample size using G*Power 3.1 (Faul, Erdfelder, Buchner, & Lang, 2009) for a within-between interaction in a repeated-measures ANOVA (effect size = 0.25 [medium], alpha = 0.05). This analysis yielded 44 as the minimum sample size. We tested a total of 90 participants, and after exclusions (see below), our final sample size included 59 participants.

Children with TD were recruited from the Greater Boston area via mailings. Children diagnosed with ASD were recruited through local early intervention agencies and participation occurred at the beginning of the visit in which diagnostic testing was later performed.

For children with ASD, clinical diagnosis was assigned by a licensed psychologist using the Autism Diagnostic Observation Schedule-2 (Lord, Rutter, et al., 2012; Lord, Luyster, Gotham, & Guthrie, 2012) (Toddler Module, N = 20; Module 1, N = 8; Module 2, N = 1). Calibrated severity scores (CSS) were calculated using the method described by Esler et al. (2015) (Toddler Module) and Hus et al. (2014) (Module 1 and 2). Children

with ASD also were assessed using the Mullen Scales of Early Learning (MSEL; Mullen & others, 1995). For children with TD, typical development was verified through parental report, Early Learning Composite standard score (ELC) on the MSEL, and scores on the Brief Infant–Toddler Social and Emotional Assessment (BITSEA) (Briggs-Gowan, Carter, Irwin, Wachtel, & Cicchetti, 2004). An ELC on the MSEL below 70 is 2 SD below the standardized mean and equivalent to a “well below average” level of cognitive development. Children who did not meet criteria for ASD (7 children) or TD (9 children) were excluded. Participants had no known vision impairments (1 ASD child excluded) or first-degree relatives with colorblindness (2 TD children excluded).

Forty-six children with TD and forty-four children diagnosed with ASD were tested. Twenty-two children (13 TD, 11 ASD) were excluded because of poor eye-track quality (see Data Analysis), 4 children (1 TD; 3 ASD) were excluded because of experimental error, 2 children with TD were excluded because of parental interference, and one child diagnosed with ASD was excluded for failing to attend to the target during the training phase (see below for details).

The final participant sample was 30 children with TD and 29 children diagnosed with ASD. Participants’ age ranged from 15 to 37 months (ASD: $M = 27.39$, $SD = 4.50$; TD: $M = 27.34$, $SD = 5.80$). Table 3 shows a summary of participants’ demographic information and assessment scores.

Table 3. Summary of participants' demographic information and scores on standardized assessments in Experiment 3.

| | ASD | TD |
|------------------------|---------------|----------------|
| N | 29 | 30 |
| # Females | 1 | 17 |
| Age (months) | 27.39 (4.50) | 27.34 (5.80) |
| range | 19-37 | 15-37 |
| Valid trials collected | 18.90 (1.29) | 19.33 (1.15) |
| Ethnicity (# children) | | |
| Hispanic or Latino | 15 | 6 |
| Not Hispanic or Latino | 9 | 21 |
| Not reported | 3 | 0 |
| Mullen Scales: | | |
| VR | 35.81 (9.92) | 57.62 (10.75) |
| FM | 33.04 (9.97) | 48.07 (7.74) |
| RL | 24.15 (10.55) | 54.03 (12.50) |
| EL | 29.12 (9.01) | 54.86 (10.85) |
| ELC | 64.77 (12.84) | 107.41 (15.60) |
| ADOS-2: | | |
| SA CSS | 7.97 (1.96) | - |
| RRB CSS | 8.71 (1.19) | - |
| Total CSS | 8.74 (1.44) | - |

Note. T scores ($M = 50$, $SD = 10$) were reported for the following MSEL scales: Visual Reception, (VR), Fine Motor (FM), Receptive Language (RL), and Expressive Language (EL). The Early Learning Composite (ELC) standard score ($M = 100$, $SD = 15$) was

computed from these four scales, and reflects general cognitive ability. TD children in our sample scored significantly higher than children with ASD on the MSEL ELC ($t(53) = -10.991; p < .001, d = 2.984$). ADOS-2 Social Affect (SA), Restricted, Repetitive Behavior (RRB), and Total (Total) Calibrated Severity Scores (CSS) were measured for children diagnosed with ASD. Values represent mean and (SD).

Apparatus

Visual stimuli were displayed on a 17-inch LCD Tobii T120 eye-tracker via Tobii Studio's presentation software (Tobii Technology, Stockholm, Sweden). Sounds were played through external speakers centered behind the display. Participants were observed via a video camera on top of the screen and looking behavior during testing was monitored on Tobii Studio's Live Viewer. Eye movements were recorded at 60 Hz.

Stimuli & Procedure

Toddlers were seated on their caregiver's lap, approximately 55–65 cm from the screen (see Figure 13). Caregivers wore blacked-out sunglasses or kept their eyes closed, and were instructed not to talk to the child. The experiment began with a 5-point calibration procedure, after which the visual search task commenced.

Search items were color-rendered photographs of apples ($5 \times 5^\circ$) and carrots ($2 \times 8^\circ$). Targets were real-world color/shape combinations (i.e., a green apple and an orange carrot) and distractors were novel and opposite color/shape combinations (i.e., a green

carrot and an orange apple). Search items were presented on a gray background with a 2° fixation cross and arranged inside a 23° diameter circle.

Trials were divided into five phases and were presented as follows:

Familiarization (2 trials), Training (3 trials), Baseline (5 trials), Switch-1 (5 trials), Switch-2 (5 trials) (see Figure 1b). *Familiarization* arrays consisted of all four stimuli types in a square configuration. *Training* arrays were single-feature search displays (color or shape) and consisted of a target and a set of 7 homogenous distractors (green carrots or orange apples). Training arrays were presented to highlight the special status of the target through ‘pop-out’ prior to the baseline phase (Kaldy, et al., 2011; Treisman & Gelade, 1980). Target detection in single-feature trials based on color or shape attributes does not require effortful search and is highly efficient (Wolfe & Horowitz, 2004). *Baseline and Switch arrays* were feature conjunction displays and consisted of two potential feature conjunction targets (one green apple and one orange carrot), and 6 distractors (3 orange apples, 3 green carrots). Target detection in this context requires effortful or inefficient search (Wolfe & Horowitz, 2004). The two potential targets were located equidistant from the center of the screen.

On each trial (except during the Familiarization phase), the T_R moved into the center of the screen (~1 s) while a cartoon airplane sound effect played, and then bounced up and down for ~1 s while a cartoon honking sound effect played. The T_R then disappeared and the search array appeared for 4 s (search period). Then, the T_R rotated back and forth for ~2 s accompanied by a cartoon applause sound effect (reward

animation). During the Familiarization phase, the search array merely appeared for 4 s. In the inter-trial interval (4 s) a tick-tock sound played. The entire task lasted approximately 5 min 30 s.

To assess attentional set-shifting, we manipulated which of the two targets was ‘relevant’ in each phase. We did this by using nonverbal cues: the currently relevant target (T_R) was animated prior to the search period and immediately after it. The other target (irrelevant target, T_{IR}) remained static. During the baseline phase, toddlers were tasked with finding the T_R , and during switch phases, this rule reversed: the T_R became the T_{IR} and the T_{IR} became the T_R . This rule reversal occurred twice (i.e., every 5 trials, Switch-1 and Switch-2) and remained in effect until the next rule reversal. The identity of the T_R during baseline (green apple or orange carrot) was counterbalanced across participants. The quadrant of the T_R (upper left, upper right, lower left, lower right) was always next to the quadrant of the T_{IR} and was counterbalanced across trials with the constraint that it never occupied the same quadrant 1-trial-back.

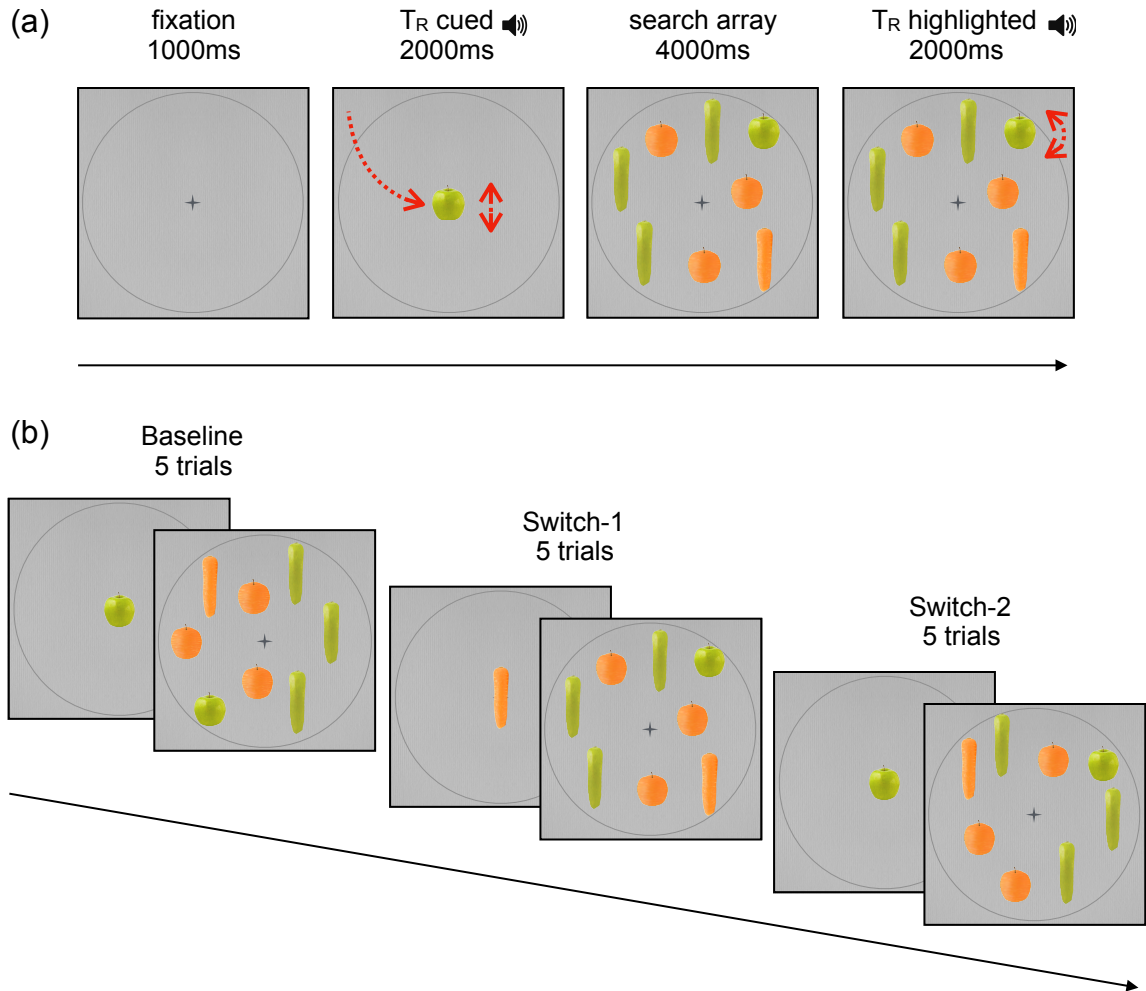


Figure 13. Experiment 3 trial structure and example stimuli. Toddlers were tasked with searching for the relevant target (T_R). Panel (a) shows the event sequence within a trial. Animations are depicted in red. Each trial began with a fixation cross, followed by the T_R cue. The search array was then displayed for 4 secs, after which the T_R began to rotate. Panel (b) shows the experimental design. During the Baseline phase, toddlers were tasked with finding the T_R . This rule reversed during the switch phase: the T_R became the T_{IR} and the T_{IR} became the T_R .

Data analysis

Gaze positions were averaged between the two eyes to reduce noise. Fixations were defined using the Tobii I-VT filter, which classifies eye movements based on the velocity of the directional shifts of the eye (Olsen, 2012). Participants whose overall track quality was low (having less than 60% of eye-tracking samples) were excluded from analyses. Areas of interest (AOIs) were defined for all search array items (Figure 14). Data from trials with a fixation duration to the screen shorter than 100 ms or less than one AOI fixated were excluded. There was no significant difference in the average number of valid trials retained (out of 20) between children with ASD or TD (ASD: $M = 18.28$, $SD = 1.56$; TD: $M = 18.83$, $SD = 1.46$; $t(57) = -1.418$, $p > .05$, $d = .364$) or the average time spent fixating the screen (ASD: $M = 2791$ ms, $SD = 403$ ms; TD: $M = 2906$ ms, $SD = 384$ ms; $t(57) = 1.126$, $p > .05$, $d = .293$).

There were three variables of interest. Hit rate was defined as the proportion of trials on which the T_R (or T_{IR}) was fixated. Fixation duration, defined as the average total looking time to the T_R (or T_{IR})⁴. Average hit rate to distractors was included in analyses to serve as a reference. Fixation latencies were defined as the time duration between the first fixation to the screen and the first fixation within a target AOI (T_R or T_{IR})⁵. We focused

⁴ If an AOI type was not fixated in an entire phase, the value equivalent to the participants' grand average fixation duration to all items was substituted for the missing value (ASD = 12.32% trials; TD = 12.38% trials).

⁵ To facilitate statistical analysis, if a target was not fixated during an entire phase, average fixation latencies was equivalent to the average fixation latency to either target for the entire experiment (ASD = 12.32% trials; TD = 12.38% trials).

our analyses on hit rates to the two potential targets as our main measure of successful search (Kaldy et al., 2011), and fixation durations to the two potential targets as our measure of task understanding. Classic visual search paradigms measure reaction time in target-present vs. target-absent trials and the efficiency of the search is measured as the slope of the function relating RT and set size (Treisman & Gelade, 1980; Wolfe & Horowitz, 2004, 2017). In the current version of the task set size was not varied, thus we did not expect fixation latency (time-to-target) to be influenced by our manipulations.

Data were assessed for violations of assumptions of normality and sphericity. Degrees of freedom were corrected using Huynh-Feldt estimates of sphericity when appropriate. All post-hoc tests were Bonferroni corrected.

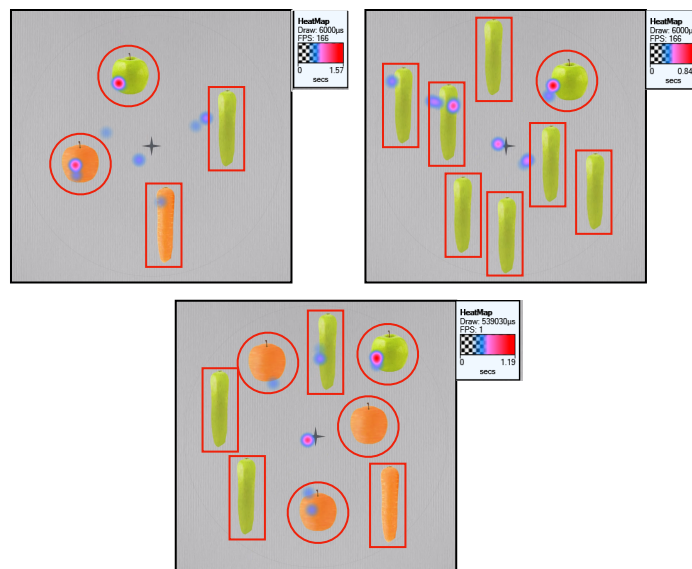


Figure 14. Experiment 3 areas of interest. Areas of interest are outlined in red. Heat map of total fixation duration to the search array items during a Familiarization trial (top left), a Training trial (top right), and a Baseline trial (bottom center) for a single TD participant.

Results

Training phase

To determine whether toddlers looked at the T_R more frequently than a distractor, hit rates were assessed via a 2 (Group: ASD vs. TD) \times 2 (Item type: T_R vs. Distractor) mixed ANOVA. Results showed a main effect of Item type ($F(1, 57) = 328.344, p < .001, \eta_p^2 = .853$); a main effect of Group ($F(1,57) = 4.319, p = .042, \eta_p^2 = .070$); and no interaction between Group and Item type ($F(1,57) = .152, p > .05, \eta_p^2 = .067$). T_R hit rate (87.57%) was higher than distractor hit rate (34.22%). The percentage of items visited over the search period was lower for toddlers with ASD (56.5%) than toddlers with TD (63.9%) (see Figure 15a).

To determine whether toddlers preferentially attended to the T_R and successfully followed the nonverbal instructions of our procedure, fixation durations were assessed via a 2 (Group: ASD vs. TD) \times 2 (Item type: T_R vs. Distractor) mixed ANOVA. Results showed a main effect of Item type ($F(1, 57) = 39.233, p < .001, \eta_p^2 = .408$); no main effect of Group ($F(1,57) = .196, p > .05, \eta_p^2 = .003$); and no interaction between Group and Item type ($F(1,57) = .342, p > .05, \eta_p^2 = .006$). On average, the T_R was fixated longer (829 ms) than a distractor (524 ms) (see Figure 15b).

Attentional set-shifting

To compare the frequency with which toddlers looked at the T_R before and after a target-switch, hit rates were assessed via a 2 (Group: ASD vs. TD) \times 3 (Item type: T_R vs.

T_{IR} vs. Distractor) x 3 (Phase: Baseline vs. Switch-1 vs. Switch-2) mixed ANOVA. Results showed a significant main effect of Item type ($F(1.746, 99.511) = 29.188, p < .001, \eta_p^2 = .339$); and a main effect of Phase ($F(2, 114) = 6.329, p = .002, \eta_p^2 = .100$); but no significant main effect of Group ($F(1, 57) = 1.177, p > .05, \eta_p^2 = .020$) and no significant interaction effects (all $F_s \leq 1.419, p_s \geq .239, \eta_p^2 \leq .024$). Post-hoc tests were conducted to further explore the main effects of Item type and Phase. T_R hit rate was higher than T_{IR} hit rate ($p < .001, d = .834$) and higher than distractor hit rate ($p = .024, d = .359$). T_{IR} hit rate was lower than distractor hit rate ($p < .001, d = .794$). Fixation rates (percentage of all items visited) did not change from Baseline to Switch-1 ($p > .05, d = .074$), but were lower during Switch-2 compared to Baseline ($p = .023, d = .360$) (see Figure 15a).

To determine whether toddlers preferentially attended to the T_R across the three phases of the study, fixation durations were assessed via a 2 (Group: ASD vs. TD) x 3 (Item type: T_R vs. T_{IR} vs. Distractor) x 3 (Phase: Baseline vs. Switch-1 vs. Switch-2) mixed ANOVA. Results showed a main effect of Item type ($F(1.619, 92.280) = 19.206, p < .001, \eta_p^2 = .252$); no main effect of Phase ($F(1.847, 105.273) = .825, p > .05, \eta_p^2 = .014$); and no main effect of Group ($F(1, 57) = .147, p > .05, \eta_p^2 = .003$). There was a significant interaction between Item type and Phase ($F(3.763, 214.486) = 3.177, p = .017, \eta_p^2 = .053$) and all other interaction effects were non-significant (all $F_s \leq 1.249, p_s \geq .284, \eta_p^2 \leq .021$).

Post-hoc tests were conducted to further explore the interaction effect. First, we compared Item type across Phases. T_R fixation duration was not significantly different at Baseline compared to Switch-1 ($p > .05$, $d = .263$) or Switch-2 ($p > .05$, $d = .032$). T_{IR} fixation duration was shorter at Baseline compared to Switch-1 ($p = .029$, $d = .349$) and not significantly different at Baseline compared to Switch-2 ($p > .05$, $d = .208$). Average distractor fixation duration was not significantly different across phases (all p s $\geq .505$, $d \leq .179$). Then, we compared Item type within each phase. At Baseline, the T_R was fixated longer than the T_{IR} ($p < .001$, $d = .657$) and distractors ($p = .001$, $d = .536$). It is important to note that during Baseline, the T_{IR} was not previously relevant and so was equivalent to a regular distractor in this respect. At Baseline, the T_{IR} fixation duration was also not different from that of distractors ($p > .05$, $d = .251$). At Switch-1, the T_R fixation duration was not different from T_{IR} fixation duration ($p > .05$, $d = .112$) or that of distractors ($p > .05$, $d = .256$), and T_{IR} fixation duration was not different from that of distractors ($p > .05$, $d = .151$). At Switch-2, the T_R was fixated longer than the T_{IR} ($p = .003$, $d = .458$) and distractors ($p = .008$, $d = .412$). T_{IR} fixation duration was not different from distractors ($p > .05$, $d = .077$) (see Figure 15b).

Finally, we report the results from our fixation latency analysis (see Figure 16). There was a main effect of Target type, $F(1, 57) = 4.255$, $p = .044$, $\eta_p^2 = .069$; no main effect of Phase, $F(2, 114) = .121$, $p = .886$, $\eta_p^2 = .002$; no main effect of Group, $F(1, 57) = .084$, $p = .773$, $\eta_p^2 = .001$; and an interaction between Target type and Phase, $F(2, 114) =$

4.810, $p = .010$, $\eta_p^2 = .078$. All other interaction effects were non-significant, all $F \leq 2.055$, $p \geq .133$, $\eta_p^2 \leq .035$. Post-hoc testing (Bonferroni) revealed no significant difference between average fixation latency to the TR and the TIR at Baseline, $p = .531$, or at Switch-1, $p = .930$. At Switch-2, average fixation latency to the TR was shorter than average fixation latency to the TIR, $p < .001$.

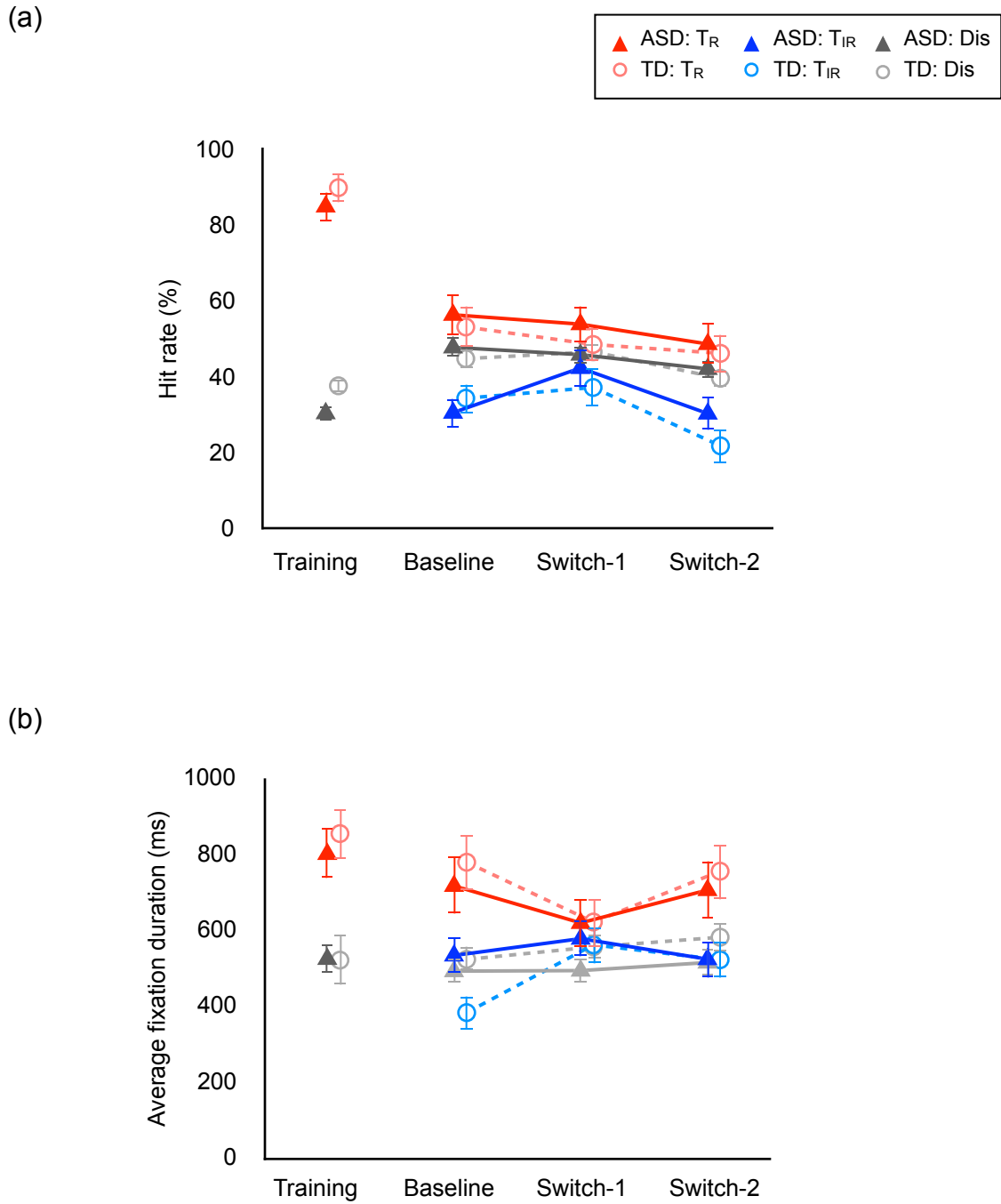


Figure 15. Experiment 3 hit rates (a) and average fixation durations (b) for the T_R, the T_{IR}, and Distractors. Bars are 1 standard error.

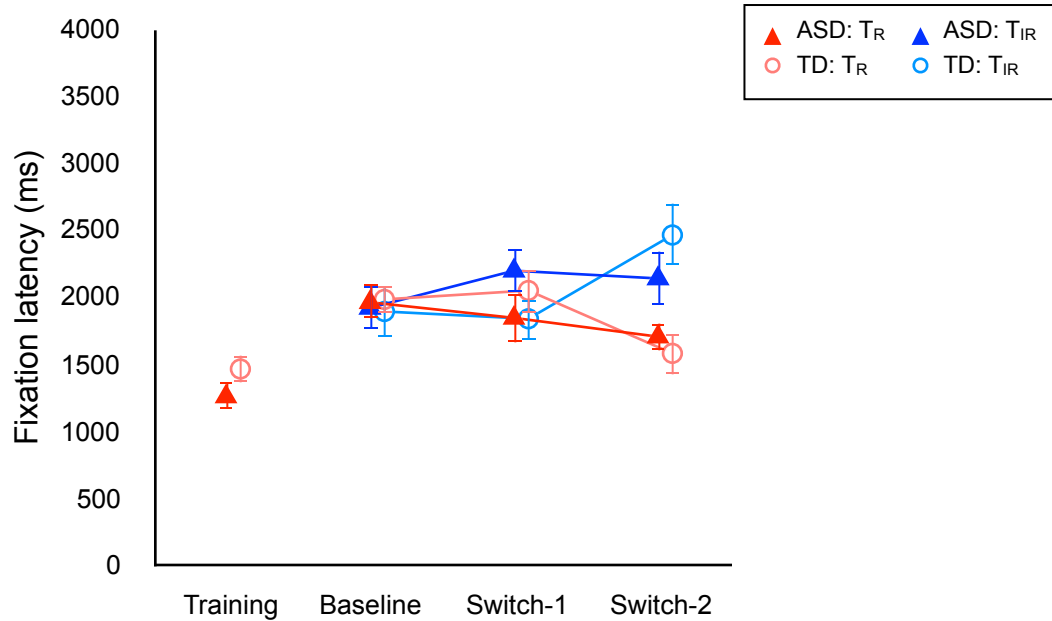


Figure 16. Experiment 3 fixation latency for the T_R and the T_{IR}. Bars are 1 standard error.

Relations with participant characteristics

Although our two groups of toddlers were age-matched (see Table 3), their age range spanned 22 months. Thus, we tested whether the developmental trajectory of attentional set-shifting differed between toddlers with ASD and TD. We also tested whether performance on our task was related to mental age and ASD symptom severity. For each participant, we computed their ‘switch cost’ (SC) following each of the two target switches by calculating the change in performance related to T_R. We subtracted performance at Baseline from Switch-1 performance (SC-1), and Baseline from Switch-2 performance (SC-2). Thus a negative score indicated a decrease in performance (i.e., a greater switch cost). For each group, Pearson’s correlations were computed between Age

(in days), MSEL sub-scale T-scores (Visual Receptive, Fine Motor, Receptive Language, Expressive Language), ADOS-2 CSS scores (Social Affect, Restricted Repetitive Behavior, Total; ASD group only) and switch cost scores (Table 4). The strength of the relationships in the two groups was compared using Fisher's z-transformation. For toddlers with ASD, there was a negative relationship between Age and fixation duration SC-1, $r = -.371, p = .047$ (Figure 17a). There was also a positive relationship between Expressive Language and fixation duration SC-1 in the ASD group, $r = .439, p = .025$ (Figure 17b). For the toddlers with TD, Visual Reception was positively related to hit rate SC-2, $r = .542, p = .002$, and fixation duration SC-2, $r = .478, p = .009$, and Receptive Language to fixation duration SC-2, $r = .472, p = .010$. None of our experimental measures were related to clinical symptoms in the ASD group.

Table 4. Pearson's correlations between switch cost and participant characteristics.

| | <u>Hit rate</u> | | | | <u>Fixation duration</u> | | | |
|------------------|-----------------|-----------|---------------|---------------|--------------------------|-----------|--------------|---------------|
| | <u>SC-1</u> | | <u>SC-2</u> | | <u>SC-1</u> | | <u>SC-2</u> | |
| | ASD | TD | ASD | TD | ASD | TD | ASD | TD |
| Age ^a | -0.9 | 0.041 | 0.01 | 0.031 | -.371* | -0.074 | -0.261 | 0.01 |
| VR ^b | 0.106 | 0.232 | <u>0.046</u> | <u>.542**</u> | 0.276 | 0.119 | <u>-0.19</u> | <u>.478**</u> |
| FM ^c | 0.005 | 0.041 | 0.009 | -.130 | 0.26 | -0.04 | 0.131 | -0.054 |
| RL ^d | -0.206 | 0.12 | <u>-0.131</u> | <u>.472**</u> | 0.176 | 0.02 | -0.248 | 0.097 |
| EL ^e | -0.214 | 0.096 | -0.198 | 0.267 | .439* | 0.072 | -0.18 | 0.184 |
| SA ^f | 0.127 | | -0.112 | | -0.024 | | 0.145 | |
| RRB ^g | -0.037 | | -0.037 | | -0.198 | | -0.111 | |
| CSS ^h | -0.089 | | -0.089 | | -0.067 | | 0.107 | |

Note. Switch cost (SC) was defined for the change in performance for the T_R following each of the two target switches. We subtracted performance at Baseline from Switch-1 performance (SC-1), and Baseline from Switch-2 performance (SC-2). * Correlation is significant at the 0.05 level (2-tailed). ** Correlation is significant at the 0.01 level (2-tailed). Fischer r-to-z transformation was conducted to test the significance of the difference between group correlation coefficients. Significant comparisons at the 0.05 level are underlined (2-tailed). ^a Age in days. ^b MSEL Visual Receptive. ^c MSEL Fine Motor. ^d MSEL Receptive Language. ^e MSEL Expressive Language. ^f ADOS-2 Social Affect domain Calibrated Severity Score. ^g ADOS-2 Restricted, Repetitive Behavior domain Calibrated Severity Score. ^h ADOS-2 Total Calibrated Severity Score.

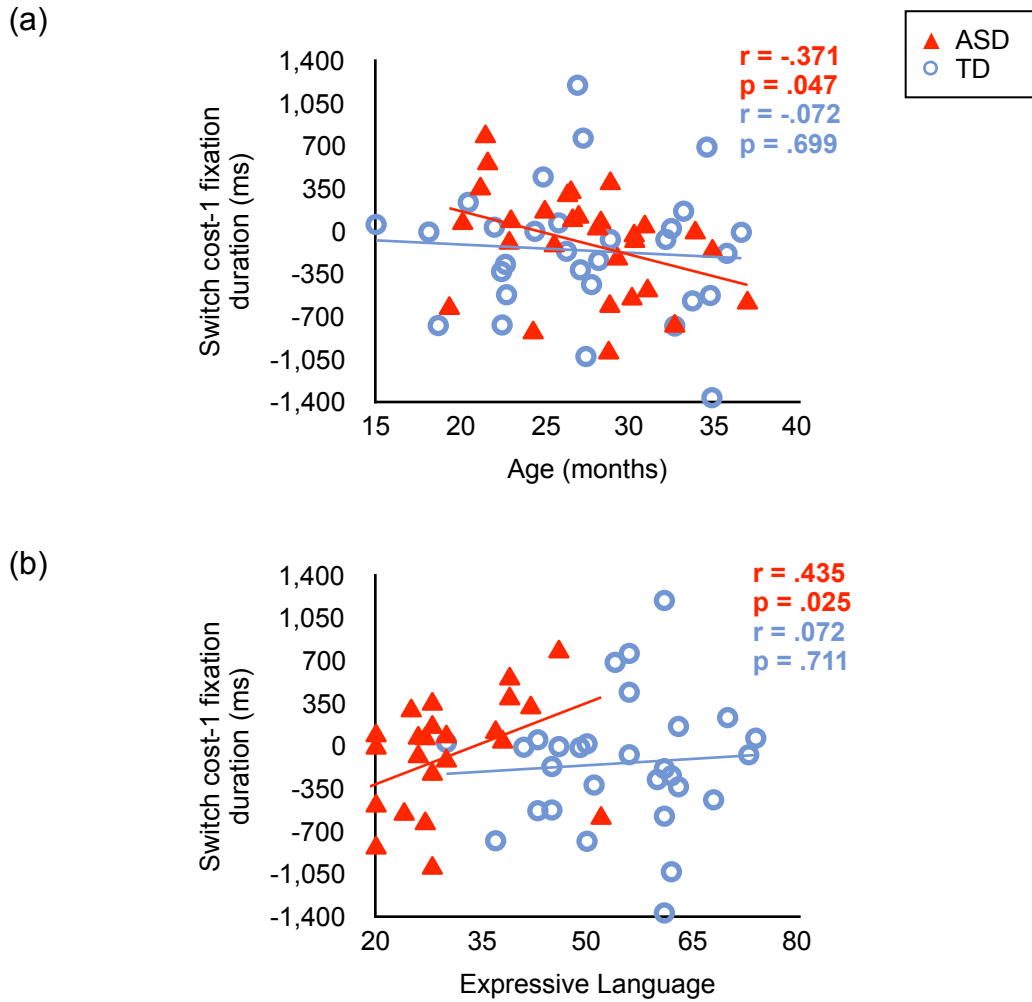


Figure 17. Relations between participant characteristics and SC-1 fixation duration in Experiment 3.

Discussion

Here, we employed a novel nonverbal eye-tracking visual search paradigm to test attentional set-shifting in very young toddlers with and without ASD. Contrary to the findings from studies with preschool-age children (e.g., McEvoy et al., 1993; Pellicano et al., 2017), we found no evidence of impaired attentional set-shifting in ASD at this age.

In our experiment, toddlers were tasked with searching for one of two potentially relevant targets using nonverbal cues and switching this rule. At Baseline, both groups of toddlers found the T_R more often, and fixated it longer, than the T_{IR} . Importantly, following the *first* target switch, both groups of toddlers found the T_R more often than the T_{IR} , although neither group fixated the T_R significantly longer than the T_{IR} . Following the *second* target switch, both groups of toddlers found the T_R more often, and fixated it longer, than the T_{IR} . In short, both groups could switch targets, and the performance of toddlers with ASD did not differ from age-matched TD controls. The lack of a performance difference between our groups is striking, given that the toddlers with ASD in our sample had significantly lower mental age than our age-matched controls (ELC: ASD: $M = 64.77$, $SD = 12.84$; TD: $M = 107.41$, $SD = 15.60$, $p < .001$, $d = 2.984$) and had moderate-to-severe ASD symptoms.

We also explored whether attentional set-shifting performance was related to participant characteristics. None of our experimental measures were related to clinical symptoms in ASD. However, for toddlers with ASD, there was a significant relationship between chronological age and switch cost at the first switch: that is, older toddlers with ASD demonstrated a greater switch cost. This trend of emergence is consistent with the existing literature on executive control deficits being present in ASD in the preschool period. There was also a positive relationship between expressive language ability and switch cost at the first switch, revealing that toddlers with weaker language skills demonstrated a greater switch cost. However, given these relationships were specific to

the fixation duration measure, we believe it would be premature to draw any strong conclusions from these findings.

Behavioral inflexibility is a central feature of ASD and is a major barrier to social interaction and learning. To date, investigations of set-shifting in ASD have yielded inconsistent findings. Studies employing complex attentional set-shifting paradigms (such as the DCCS) have suggested that the development of this ability is already delayed in early childhood, whereas studies with simple response set-shifting have suggested deficits are later emerging and thus secondary to the development of core symptoms of ASD. As our task was a feature-conjunction search, to perform well, toddlers needed to maintain an attentional set that included the relevant target features (e.g., green/apple), and update it following a target switch (e.g., orange/carrot). Toddlers were not “instructed” to ignore the previous but now irrelevant target. Thus, we can conclude that when the verbal and inhibitory control demands of a task are low, young toddlers with ASD do not exhibit an impairment in attentional set-shifting.

How might we reconcile the findings from the current study with our knowledge of the development of brain mechanisms underlying attentional set-shifting? In the typical adult brain, successful set-shifting is dependent on a fronto-parietal central executive network, which consists of the ventrolateral prefrontal cortex, inferior frontal cortex, posterior parietal cortex, anterior insula, and the anterior cingulate cortex (Cole & Schneider, 2007; Dajani & Uddin, 2015; Duncan, 2010). In young TD children, fNIRS studies have found that differences in the activation of the prefrontal cortex (Moriguchi &

Hiraki, 2013) and interactions between frontal and posterior parietal regions (Buss & Spencer, 2017) mediate successful set-shifting.

While the neural mechanisms of attentional set-shifting in young children with and without ASD has yet to be contrasted, recent evidence suggests atypical functional connectivity of the dorsal and ventral attention networks from infancy to adolescence in ASD (Elison et al., 2013; Farrant & Uddin, 2016; Keehn et al., 2013). Selective attention is essential for successful set-shifting and future research should examine how the early development of this system affects executive control in ASD.

Our findings extend the developmental executive control literature in two important ways. First, we introduced a novel eye-tracking task to measure attentional set-shifting performance that can be used with children under 3 years of age. To date, the youngest age at which attentional set-shifting has been studied in TD toddlers, using verbal instructions, was at 30 months (Blakey & Carroll, 2017; Blakey et al., 2016). Our task does not require verbal instructions or response, reducing the effect of verbal fluency on performance, and making it ideal for studying young or atypically developing populations. Furthermore, our paradigm is based on gaze behavior. Previous research has shown that eye-tracking is a sensitive measure of attentional differences between children with and without ASD (Guillon, Hadjikhani, Baduel, & Roge, 2014; Karatekin, 2007). To date, the use of eye-tracking to study attentional set-shifting has been limited to older TD children and adults (Chevalier, Blaye, Dufau, & Lucenet, 2010; Chevalier et al., 2017).

Second, in this novel paradigm with low task demands, both children with TD and ASD showed successful attentional set-shifting at 2 years of age.

It is remarkable that toddlers with ASD performed as well as the age-matched TD controls in our task, given the substantial difference in cognitive developmental level. That said, we did not see a significant ‘ASD advantage’ in visual search during Baseline as expected from prior work (Kaldy, et al., 2013) and in contrast to findings with a similar paradigm (Kaldy et al., 2011). To ensure the search array items were equally perceptually salient, we rendered all items nominally isoluminant to each other and the background (thus, only hue differences remained between the items). Attention to color (hue) differences has been shown to be impaired in children with ASD (Franklin et al., 2010; Franklin, Sowden, Burley, Notman, & Alder, 2008). Thus one possible explanation for the lack of an ASD advantage here is that the current stimulus parameters, where color (hue) information was more critical, affected the search strategies of our toddlers with ASD more so than toddlers with TD.

Attentional set-shifting is necessary for many higher-order cognitive tasks, and our study represents the first step in studying it in young toddlers with typical and atypical development. In a novel paradigm with low task demands, at 2 years of age, both typically developing toddlers and those diagnosed with ASD demonstrated this crucial executive control ability. Our findings suggest that despite clear problems with behavioral flexibility, deficits in attentional set-shifting are not a central feature of ASD at the earliest age the condition can be diagnosed.

CHAPTER 4

GENERAL DISCUSSION

Attention is essential for efficient information processing and fundamental in shaping our experience of the world. For the developing mind, the link between attention and experience is key: attention alters what children experience and learn about their world thereby shaping cognitive development (Colombo, 2001; Ruff & Rothbart, 2001).

Attentional differences have long been associated with ASD and are increasingly being implicated in the etiology of the disorder (M. H. Johnson et al., 2015; Keehn et al., 2013). Furthermore, attentional differences appear to be extensive in ASD (Ames & Fletcher-Watson, 2010) and attentional differences in the first year of life are one of the earliest behavioral indications of an ASD diagnosis in early childhood (Elsabbagh & Johnson, 2016; M. H. Johnson et al., 2015; Osterling & Dawson, 1994). Research into the typical and atypical development of attention during the toddler period has been limited by methodological constraints: toddlers pose a measurement problem — too old for looking-based measures of attention that are regularly used with infants, yet too young to reliably follow verbal instructions or pay attention for long periods of time, as required by attention paradigms used with children or adults.

The goal of this thesis was to address this “toddler-gap” in our understanding of attention in typical development and ASD. Experiment 1 and Experiment 2 demonstrated that when selective attention is directed elsewhere, that is, in service of searching for a pre-defined target, attention to a novel task-irrelevant oddball may be atypical in toddlers with ASD depending on stimulus properties. In Experiment 1, there were no differences in how toddlers with ASD and TD toddlers attended to a novel onset oddball. However, in Experiment 2, TD toddlers appeared to prioritize the novel colored oddball to a greater extent than ASD toddlers. Experiment 3 demonstrated that attentional set-shifting in the context of visual search can be typical in toddlers with ASD. Together, these findings provide insight into and raise several interesting questions about the development of attention in ASD. Table 5 provides a summary of the fixation duration results.

Table 5. Summary of fixation duration results from Experiment 1, 2, and 3.

| Phase | Oddball | Task relevance | Novelty | Fixation Duration |
|-----------------|------------------------------|-----------------------|----------------|--------------------------|
| Exp. 1 Oddball | novel onset | irrelevant | novel | ASD = TD |
| Exp. 2 Oddball | novel color | irrelevant | novel | ASD < TD |
| Exp. 3 Baseline | opposite feature-conjunction | irrelevant | novel | ASD = TD |
| Exp. 3 Switch-1 | opposite feature-conjunction | previously relevant | old | ASD = TD |

Selective attention in toddlers with ASD

Selective attention in the real world involves the interaction of exogenous stimulus-driven and endogenous goal-driven control processes. Yet only a limited number of studies have investigated endogenous control in young children with ASD. Currently, our understanding of the development of selective attention in ASD has been informed primarily by tasks that measure exogenous orienting in ‘task-free’ passive viewing contexts (M. H. Johnson et al., 2015). The claim has been that selective attention is ‘sticky’ — children with ASD show impairments in attentional disengagement as well as reduced exploration of visual scenes (Elsabbagh & Johnson, 2016; Sacrey et al., 2014). However, empirical evidence for this claim is mixed (Fischer et al., 2016, Robertson, et al., under review). In TD children, weak endogenous control of attention is believed to underlie increased distractibility (Rothbart & Posner, 2015). However, it may also ensure young children do not miss potentially important opportunities for learning about their world. In adults, attention is primarily controlled by endogenous factors (Bacon & Egeth, 1994; Folk et al., 1992; Jonides & Yantis, 1988; Stoppel et al., 2013; Theeuwes, 2010) and thus information that is not within the attentional set is often ignored, even if this information is in fact relevant.

The findings from Experiment 1 and Experiment 2 extend the selective attention literature in three important ways. First, when attention is goal-directed (in search of a pre-defined target), attentional modulation by a task-irrelevant novel stimulus depends on perceptual properties. Previous research has suggested attention to stimuli defined by a

novel onset is impaired in older children and adults with ASD (Greenaway & Plaisted, 2005; Keehn & Joseph, 2008). However, in Experiment 1, we found that both groups of toddlers attended to the novel onset oddball and did so equally. The previous literature on attentional capture to task-relevant and task-irrelevant colored oddballs is more mixed. For example, Greenaway and Plaisted (2005) found that attentional modulation by a colored oddball when task-relevant (i.e., a valid cue) or task-irrelevant (i.e., a visual search distractor) was typical in older children with ASD. Keehn and others (Keehn et al., 2016, 2017) found reduced attentional capture for both colored targets and distractors, regardless of task-relevance, in children with ASD. In Experiment 2 we found toddlers with ASD attended to the irrelevant colored oddball more than a regular distractor, suggesting they noted the oddball's special status. However, relative to TD toddlers, the colored oddball item had a reduced attentional priority, suggesting attentional modulation by a unique color may be different in ASD.

Secondly, we did not observe any evidence that children with ASD explored the search array differently from TD children: median fixation duration to a regular distractor was not significantly longer for toddlers with ASD relative to TD toddlers in either Experiment 1 or Experiment 2. When attention is actively recruited in service of an ongoing task, it seems that previously observed low-level differences in gaze patterns may no longer be present. Recently, Drysdale et al. (2017) reviewed the adult eye-tracking literature on gaze-patterns in individuals with ASD during active task engagement. Typical gaze patterns were observed in tasks such as reading, memory, and

when ‘following instructions’ (e.g., an instructional video). Atypical gaze patterns were observed during word learning and driving, although behavioral performance was typical. In fact, the only situation where gaze patterns were atypical and related to task performance was in the context of imitation.

Finally, to evaluate whether atypicalities in processing task-irrelevant novel stimuli are linked to core ASD symptoms, we examined associations between attention to the novel colored oddball and behavioral observational measures of ASD-related symptoms in Experiment 2. Evidence linking a specific attentional impairment to any of the core social-communicative symptoms would lend support to theories suggesting attentional modulation atypicalities are not merely associated or secondary features of ASD but are of deeper etiological significance with regard to the defining symptoms of ASD and their neurobiological underpinnings. However, increased ASD clinical symptoms were not related to decreased attention (i.e., fixation duration) to the oddball. Interestingly, there were strong positive relationships between multiple measures of cognitive ability (Visual Reception, Fine Motor, Expressive Language, and Early Learning Composite Score). There was, however, no statistical relationship between cognitive ability and attention to the target, suggesting this effect was specific to the novel and task-irrelevant oddball and not due to longer or slower fixations more generally. The relationship between attention to the oddball and cognitive ability was not present in the TD group, suggesting developmental level may moderate attentional capture in children with ASD only.

Executive control in toddlers with ASD

The findings from Experiment 3 make an important contribution to the developmental executive control literature. Substantial empirical support for the executive control hypothesis in ASD has come from assessments of set-shifting in older children and adults with ASD (for reviews, see Demetriou et al., 2017; Geurts et al., 2009; Leung & Zakzanis, 2014). However, only a handful of studies have examined performance on set-shifting tasks in children with ASD younger than 5 years of age and these studies have yielded inconsistent findings. Studies employing complex attentional set-shifting paradigms (such as the DCCS) have suggested that the development of this ability is already delayed in early childhood (between 3 and 5 years of age), whereas studies with simple response set-shifting in 2-3-year-old toddlers did not find any deficits. If deficits are later emerging then this would suggest they are secondary to the development of core symptoms of ASD. We developed a novel nonverbal task that allowed us to measure attentional set-shifting skills for the first time in toddlers as young as 2 years of age. Contrary to the findings from studies with 3-5-year-old preschoolers using the DCCS (Pellicano et al., 2017), in Experiment 3, we found no evidence of impaired attentional set-shifting in ASD at this age.

We also explored whether attentional set-shifting performance was related to participant characteristics. None of our experimental measures were related to clinical symptoms in ASD. However, for toddlers with ASD, there was a significant relationship between chronological age and switch cost at the first switch: that is, older toddlers with

ASD demonstrated a greater switch cost. This trend of emergence is consistent with the existing literature on executive control deficits being present in ASD in the preschool period. There was also a positive relationship between expressive language ability and switch cost at the first switch, revealing that toddlers with weaker language skills demonstrated a greater switch cost. However, given these relationships were specific to the fixation duration measure, we believe it would be premature to draw any strong conclusions from these findings. Our findings suggest that despite clear problems with behavioral flexibility, deficits in attentional set-shifting are not a central feature of ASD at the earliest age the condition can be diagnosed.

Visual search in toddlers with ASD

Dominant explanations for the visual search advantage in ASD include enhanced low-level perceptual processing (Happé & Frith, 2006; Joseph et al., 2009; Mottron et al., 2006), increased attentional efficiency or focused attention (Blaser et al., 2014; Milne et al., 2013), and increased perceptual capacity (Hessels et al., 2014; Remington et al., 2009).

In the studies presented in this thesis, it is remarkable that toddlers with ASD performed as well as chronologically age-matched TD controls given the two groups exhibited substantial differences in cognitive developmental level. However, across three experiments, we did not observe a visual search advantage — toddlers with ASD performed equally well compared to our age-matched TD controls. This finding is in direct contrast to Kaldy et al. (2011) who used a similar paradigm and population, and

also contrary to several studies that report a visual search advantage in individuals across a wide range of ages (e.g. (Gliga, Bedford, et al., 2015; Joseph et al., 2009; Keehn & Joseph, 2016; Plaisted et al., 1998). Given the studies reported in the present thesis were highly similar to Kaldy et al. (2011), we can speculate about the source of the difference in findings. There is evidence visual search is neither superior nor impaired in ASD (Iarocci & Armstrong, 2014; Keehn & Joseph, 2016), so it is possible that superior performance depends on specific task properties. Table 6 presents a comparison of methodological differences between the baseline conjunction phase of experiments reported in the current thesis and Kaldy et al. (2011).

Table 6. Comparison of sample characteristics and paradigm features.

| | <u>Kaldy et al. (2011)</u> | | <u>Exp. 1</u> | | <u>Exp. 2</u> | | <u>Exp. 3</u> | |
|---------------------------------|-----------------------------------|-----------|---------------------------|-----------|---------------------------|-----------|-------------------------------|-----------|
| | ASD | TD | ASD | TD | ASD | TD | ASD | TD |
| Target hit rate | 82.7% | 56.1% | 73.5% | 73.7% | 74.3% | 75.2% | 56.5% | 53.3% |
| <u>Sample</u> | | | | | | | | |
| Age (months) | 29.5 | 29.6 | 27.4 | 26.2 | 25.6 | 28.1 | 27.4 | 27.3 |
| # Participants | 17 | 17 | 30 | 34 | 34 | 36 | 29 | 30 |
| % Females | 17.6% | 58.8% | 26.7% | 32.4% | 20.6% | 44.4% | 3.4% | 56.7% |
| Mean # trials completed / total | 8.3 / 12 | 8.2 / 12 | 4.7 / 6 | 4.7 / 6 | 5.2 / 6 | 4.9 / 6 | 4.8 / 5 | 4.5 / 5 |
| <u>Paradigm</u> | | | | | | | | |
| Target | red apple | | red apple | | red apple | | orange carrot / green apple | |
| Set size | 5, 9, 13 | | 5, 9, 13 | | 5, 9, 13 | | 8 | |
| Distractor | red oblongs / blue apples | | red oblongs / blue apples | | red oblongs / blue apples | | green oblongs / orange apples | |
| Luminosity | not controlled | | isoluminant | | isoluminant | | isoluminant | |

Note. In Kaldy et al. (2011) participants completed between 1 and 3 blocks of the experiment. We report only results from the first run of the conjunction-feature phase.

Relative to Kaldy et al. (2011), TD toddlers in Experiment 1 and 2 demonstrated better performance, while toddlers with ASD in Experiment 3 demonstrated poorer performance. There are a number of possible factors that could have contributed to these differences. First and foremost, in the present thesis, to ensure the search array items were

equally perceptually salient, we rendered all items nominally isoluminant to each other and the background (thus, only hue differences remained between the items). Attention to color (hue) differences has been shown to be impaired in children with ASD (Franklin et al., 2010, 2008). For example, Franklin et al., (2008) found that high-functioning children with ASD are less accurate when required to remember a colored target and make more errors when required to identify the colored target amongst a set of colored distractors (akin to visual search). However, children with ASD and TD children perform equally well when the target was defined by shape. Thus the current stimulus parameters, where color (hue) information was more critical, may have affected the search strategies of our toddlers with ASD more so than toddlers with TD. Furthermore, in Experiment 3, the reduced discriminability of the stimuli (i.e., green vs. orange items on a grey background) may have rendered the task especially difficult, reducing evidence of an ASD advantage. However, it is unclear why color salience manifested as an improvement in the TD group's performance in Experiment 1 and Experiment 2 (and a small reduction in ASD performance), and a reduction in the ASD group's performance in Experiment 3. Color perception in ASD is an ability that has been somewhat overlooked and further investigation into this ability is needed, especially given the role of color perception in a number of attention tasks, including visual search.

The second noteworthy difference between the present thesis and Kaldy et al. (2011) are sample differences. In the present thesis, the sample size was considerably larger than that in Kaldy et al. (2011) however the number of trials completed was higher

in Kaldy et al. (2011). It is possible that increased levels of task-engagement in toddlers with ASD (Blaser et al., 2014) meant that children either improved at the task with time (practice effects) or that TD toddlers showed poorer performance over time (fatigue effects). Furthermore, ASD is approximately 4.5 times more common among males (1 in 42) than females (1 in 189) (Christensen, 2016). Gender effects remain to be explicitly studied in the context of the visual search. However, if being male is a factor in determining the visual search advantage, the higher number of females in the TD group in Kaldy et al. (2011) could have partially accounted for the group's lower performance. In summary, future research will be needed to clarify the role of color perception, practice or fatigue, and gender on visual search in TD children and children with ASD.

Limitations and future directions

There are a number limitations in studies in the present thesis that are worthy of discussion. First, in the present thesis, our control groups were always chronologically age-matched. This meant toddlers with ASD and TD toddlers demonstrated large differences in mental age. Often, mental age matching is used when studying ASD in an effort to eliminate the effect of non-central factors such as developmental delay (Jarrold & Brock, 2004). However, matching groups on mental age results in a mismatch in terms of chronological age — a particular problem when studying young children who have radically different experiences and competencies between the first and second year of life. Determining whether developmental delay can uniquely account for the findings presented in the present thesis will be an important avenue for future research.

Second, attention may develop differently for children who receive a diagnosis of ASD and children who are also at risk for ADHD (Geurts, Verte, Oosterlaan, Roeyers, & Sergeant, 2004; Gliga, Smith, et al., 2015; K. A. Johnson et al., 2007; M. H. Johnson et al., 2015; Rommelse, Geurts, Franke, Buitelaar, & Hartman, 2011). For example, hyperactivity levels moderates visual exploration in infants at high-risk for ASD (Gliga, Smith, et al., 2015). Shorter fixation duration during visual exploration in infancy has also been associated with increased hyperactivity-inattention in early childhood (Papageorgiou, et al., 2014). Although ADHD is commonly comorbid with ASD – it is estimated that 30-50% of individuals with ASD present with ADHD symptoms (Davis & Kollins, 2012; Leitner, 2014) — diagnosis of ASD often occurs earlier than diagnosis of ADHD. Further exploration of how attention develops in different subgroups of ASD would greatly improve our understanding this system and its relation to clinical symptoms of ASD.

Third, in Experiment 3, toddlers were not “instructed” to ignore the previously relevant but now irrelevant target. Thus, we concluded that when the verbal and inhibitory control demands of a task are low, young toddlers with ASD do not exhibit an impairment in attentional set-shifting. There are a number of reasons children can err on set-shifting tasks, and failures of selective attention, working memory, and inhibitory control have been implicated (Chevalier & Blaye, 2008; Hanania, 2010; Hanania & Smith, 2010). Whether typical levels of performance are observed in toddlers with ASD

when these abilities are differentially taxed remains to be investigated (for a commentary on this issue in adults, see Van Eysen et al., 2011).

Fourth, although we manipulated set size in Experiment 1 and Experiment 2, we did not have sufficient power to examine the effects of set-size on task-irrelevant attentional capture. Lavie (1995) proposed attentional selection depends on the perceptual load (i.e., the amount of task-relevant information) of a task. In the case of low perceptual load, task-irrelevant distractors will be processed. However, in the case of high perceptual load, task-irrelevant distractors will not be processed. There is evidence that task-irrelevant distractor suppression occurs at lower loads in TD adults relative to adults with ASD (Ohta et al., 2012; Remington et al., 2009; Remington, Swettenham, & Lavie, 2012). Future research should examine the effects of set-size on attentional capture in young children with ASD to determine when enhanced perceptual capacity observed in adults with ASD emerges. For purely exploratory purposes, Figure 18 shows oddball fixation duration and oddball hit rate as a function of set size for toddlers with ASD and TD toddlers. Visual inspection of the graph suggests that the TD groups' fixation durations to the novel colored oddball in Experiment 2 may have been modulated by set size whereas the ASD groups' fixation duration may not have been.

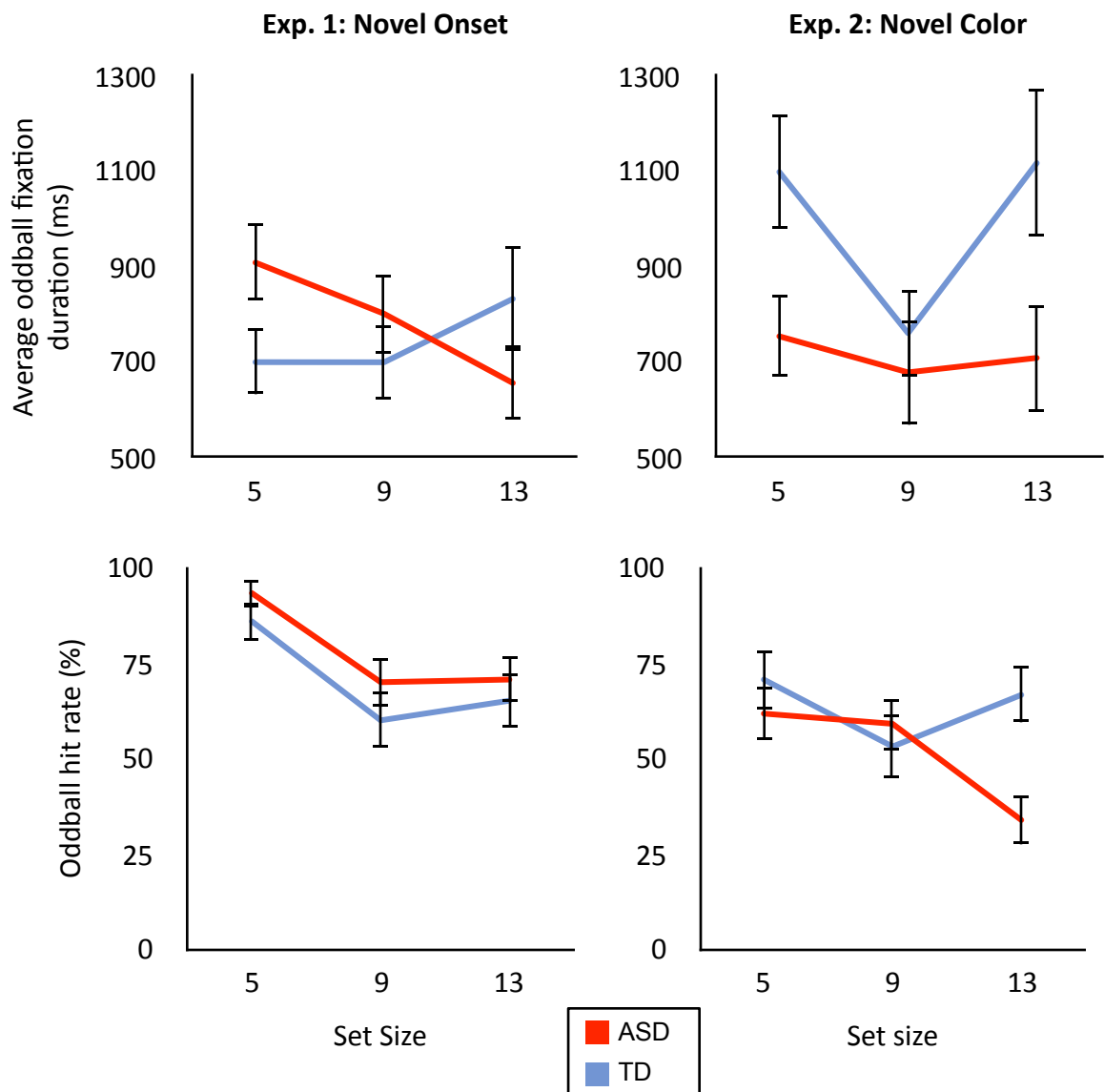


Figure 18. Average oddball fixation duration (ms) and oddball hit rate (%) by set size in Experiment 1 and 2. Bars are 1 standard error.

Fifth, it is worth considering the effect of ‘attentional set’ on task-irrelevant attentional capture. In adults, how endogenous factors interact with exogenous factors to produce attentional capture has been an area of controversy (Bacon & Egeth, 1994; Folk et al., 1992; Jonides & Yantis, 1988; Stoppel et al., 2013; Theeuwes, 2010). Stimulus-driven accounts posit that salient stimuli will capture attention regardless of the top-down attentional set of the observer (Theeuwes, 2010). By contrast, goal-driven accounts posit attentional capture depends on a shared feature (e.g. color) between the attentional set and the task-irrelevant stimulus (Folk et al., 1992). Bacon and Egeth (1994) further proposed that attentional capture depends on search mode (feature-search mode vs singleton-detection mode). It is, therefore, possible that differences in attentional set were present in toddlers with ASD and TD toddlers, and such differences were related to attentional capture. However, it is unclear how one would determine the specificity of toddlers’ attentional set in the absence of task instructions.

Finally, classic models of attentional control posit selective attention is controlled by endogenous and exogenous factors. However, more recently, it has been established that previously rewarded and/or selected stimuli are associated with increased attentional priority and automatically capture attention when task-irrelevant (B. A. Anderson, 2016; B. A. Anderson et al., 2017; Awh et al., 2012; Chelazzi et al., 2014; Jiang, 2017; Jiang et al., 2015; Munneke et al., 2016). In the present thesis, the target was animated post-search as a way to encourage children to search for this item without verbal instructions. Thus, the target may have been rewarding to toddlers, resulting in enhanced attentional

priority. In Experiment 3, following a target switch, the irrelevant target was not only previously relevant but was also previously ‘rewarded’. It is somewhat surprising then that toddlers did not demonstrate increased attentional capture by this item. This raises the question as to whether reward-driven attentional control operates the same way in young children as in adults. Finally, although atypicalities in the processing of reward and negative feedback have been observed in ASD (Broadbent & Stokes, 2013; Kohls et al., 2012; Larson, South, Krauskopf, Clawson, & Crowley, 2011; Schmitz et al., 2008), we did not find any group differences in terms of responses to the target. Future research should be directed at the effects of reward on attentional capture in young children, both with and without ASD.

Conclusions

In light of the research reviewed and the findings of the present thesis, a few thoughts can be offered. There is evidence showing that low-level differences in gaze-patterns in a free-viewing context are atypical early in life (M. H. Johnson et al., 2015). However, exogenous orienting may be typical by toddlerhood (Fischer et al., 2016, Robertson, et al., under review). Furthermore, in the Baseline phases of Experiment 1 and Experiment 2, we found no differences in gaze patterns between groups when actively engaged in a ‘classic’ feature-conjunction visual search task, suggesting that toddlers with ASD do not have impairments in their ability to move their eyes (or attention) flexibly when searching for a target.

Studies employing complex attentional set-shifting paradigms (such as the DCCS) have suggested that the development of this type of set-shifting is already delayed in early childhood in ASD, whereas studies with simple response set-shifting have suggested deficits are later emerging and thus secondary to the development of core symptoms of ASD. In Experiment 3, toddlers needed to maintain an attentional set that included a conjunction of relevant target features (e.g., green/apple), and update this representation following a target switch (e.g., orange/carrot). Toddlers were not “instructed” to ignore the previous but now irrelevant target. Thus, when the verbal and inhibitory control demands of a task are low, young toddlers with ASD do not exhibit an impairment in attentional set-shifting.

Therefore, at present, it seems atypical gaze patterns in passive viewing contexts might be useful as an early predictor of risk for ASD related symptoms in infants. However, later in life, when attention is most often under voluntary control, low-level differences in gaze patterns may no longer be a factor in developing ASD-related symptoms. Furthermore, deficits in executive control are not a primary factor in the development of behavioral inflexibility in young children diagnosed with ASD, and these deficits either emerge later or as a consequence of increased task complexity (Van Eylen et al., 2011).

Looking forward, we believe research on the development of attention in young children with ASD is essential for several reasons. First, an improved understanding of attentional differences would greatly improve characterization of a disorder diagnosed

solely on the basis of behavioral symptoms. Toddlerhood is the earliest age ASD can be diagnosed, which means findings are independent of effects of behavioral or pharmacological interventions. Second, attentional differences could underlie core symptoms, or contribute to core symptom development. Attention is pivotal to shaping experience, and in turn, cognition. Improved understanding of the link between attention and ASD symptoms would clarify neurocognitive risk factors for ASD and further elucidate the neurobiological underpinnings of these symptoms. Third, it would inform early intervention options, shown to be the most effective form of intervention. A complete understanding of the early development of attention in ASD is clearly a prerequisite for advancing the development of early behavioral markers of ASD and informing intervention options in the early childhood period.

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