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## Eye Tracking Reveals Impaired Attentional Disengagement Associated with Sensory Response Patterns in Children with Autism

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### Abstract

This study used a gap-overlap paradigm to examine the impact of distractor salience and temporal overlap on the ability to disengage and orient attention in 50 children (4–13 years) with ASD, DD and TD, and associations between attention and sensory response patterns. Results revealed impaired disengagement and orienting accuracy in ASD. Disengagement was impaired across all groups during temporal overlap for dynamic stimuli compared to static, but only ASD showed slower disengagement from multimodal relative to unimodal dynamic stimuli. Attentional disengagement had differential associations with distinct sensory response patterns in ASD and DD. Atypical sensory processing and temporal binding appear to be intertwined with development of disengagement in ASD, but longitudinal studies are needed to unravel causal pathways.

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**Author contributions** MSD and GTB initiated the idea for and design of the study, and secured funding through grants. MSD, JCB, and GTB developed the stimuli and task parameters. JCB programmed the stimuli and parameters into Tobii. MSD piloted and collected data, and tracked participants with help from research assistants. JCB extracted raw data and wrote programs to clean the data. SES conducted data management and statistical analyses in consultation with statisticians and co-authors. GTB and AB consulted on design and analyses throughout the study. All five authors contributed to the interpretation of the analysis, writing of the manuscript, and all authors read/approved the final manuscript.

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## Keywords

Autism spectrum disorder; Sensory processing; Eye-tracking; Attention; Multisensory integration; Hypo-/hyper-responsiveness

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## Introduction

Attentional control and flexibility develop throughout childhood and enable the selection of, orienting to, and processing of goal-relevant social and nonsocial stimuli, as well as behavioral regulation during periods of distress (Harman et al. 1997; Rueda et al. 2011; Ruff and Rothbart 1996). Orienting, a component of attentional control, involves the ability to disengage from an existing point of focus, make a saccade to a new stimulus, and engage with that stimulus (Johnson et al. 1991). During infancy, development of posterior brain regions associated with visual attention is thought to enhance orienting skills, as well as support sensory processing and arousal (see Colombo 2001 for a review). Deficits in orienting to social and nonsocial stimuli (Baranek et al. 2013; Dawson et al. 1998, 2004; Osterling and Dawson 1994), and disengaging attention from salient stimuli (Landry and Bryson 2004) have been demonstrated in several behavioral studies of very young children with Autism Spectrum Disorder (ASD), Autism, and Pervasive Developmental Disorder (PDD), and thus, may point to deficits in early-developing attentional control mechanisms.

Attention disengagement deficits are amongst the earliest markers in at-risk siblings of children with ASD (Bryson et al. 2007; Elison et al. 2013; Elsabbagh et al. 2009, 2013), and are predictive of a later diagnosis (Zwaigenbaum et al. 2005). Older age groups of lower-functioning adults with Autism (Kwakubo et al. 2004, 2007) and children with Autism/PDD also manifest these difficulties (Landry and Bryson 2004). However, a recent study (Fischer et al. 2013) found that children with high-functioning ASD were comparable to age- and IQ-matched peers in their speed of disengagement. Generally, though, researchers have suggested that early differences in attentional disengagement are a primary deficit in ASD and thus have cascading effects on the development of subsequent skills, including arousal regulation, visual-perception, joint attention and other social-cognitive skills (e.g., Keehn et al. 2013).

Despite behavioral evidence of aberrant attention in ASD, the underlying mechanisms are not well understood, and it remains unclear what components of visual attentional orienting are disrupted. It is also unknown to what degree deficits in attention impact other domains of impairment in ASD, such as aberrant behavioral responses to sensory stimuli, which are currently the focus of many experimental studies and treatment efforts, and are included as core symptoms of diagnostic criteria for ASD (American Psychiatric Association 2013). Attentional control is likely to interact with observable sensory response patterns in ASD because attention is affected by both top-down (e.g., cognitive resources available) and bottom-up (e.g., perceptual salience of the stimulus) influences. For example, Greenaway and Plaisted (2005), using spatial cuing and visual search tasks, showed that children diagnosed with Autism or Asperger's Disorder (ages 9.4–13.6 years) showed impaired attention for transient (i.e., onset cue) stimuli, but not for static (i.e., color cue) stimuli,

whereas typically developing same-age peers showed similar levels of attentional control regardless of stimulus type. Thus, top-down attentional deficits in children with ASD may be evident relative to controls, but only under specific stimulus conditions (e.g., sensory-perceptual properties).

Several studies of visual disengagement and orienting in ASD have examined top-down effects on attention disengagement from a central stimulus to a novel peripheral stimulus using a “gap-overlap paradigm,” but did not manipulate the bottom-up sensory-perceptual salience of the central stimuli. Instead these tasks have involved only one type of stimulus, either dynamic/animated stimuli (e.g., Elsabbagh et al. 2009, 2013; Landry and Bryson 2004) or static images (Kawakubo et al. 2004, 2007), or static images in either social or nonsocial contexts (Elison et al. 2013). Furthermore, these studies present unimodal stimuli (visual images without an auditory component), which limits understanding of cross-modality integration processes that are critical for participation in naturalistic multisensory environments. Indeed, there is some evidence that multisensory integration and attention interact atypically in high-functioning adults with ASD (Magnée et al. 2011). We argue that attentional disengagement may be particularly challenging for individuals with ASD with clinically elevated sensory symptoms (e.g., hyper/hypore-sponsive patterns) under conditions where the central stimuli are highly salient and/or multisensory in nature. Thus, research is needed to further characterize attentional control in children with ASD by examining the impact of stimulus salience, modality, and timing on the ability to disengage from one stimulus and orient attention to a new stimulus, and determine the association of putative attentional deficits to clinical symptoms.

Unusual behavioral responses to sensory stimuli are noted across modalities within both social and nonsocial contexts, and are often described as constellating into various behavioral response patterns (Ausderau et al. 2014b), including *hyporesponsiveness*: diminished or delayed response (e.g., Baranek et al. 2013; Ben-Sasson et al. 2007); *hyperresponsiveness*: exaggerated, aversive, or avoidant responses (e.g., Baranek et al. 2007; Ben-Sasson et al. 2009a; Schoen et al. 2008); *seeking*: intense sensory interests, cravings or repetitions (e.g., Ausderau et al. 2014b; Ben-Sasson et al. 2007; Liss et al. 2006); and *enhanced perception*: acute awareness (e.g., Happé and Frith 2006; Mottron et al. 2009). These sensory response patterns are prevalent in ASD across the lifespan (Baranek et al. 2006; Ben-Sasson et al. 2009b; Crane et al. 2009; Liss et al. 2006), and often co-occur within individuals with ASD (Ausderau et al. 2014a, b; Baranek et al. 2006; Ben-Sasson et al. 2008; Liss et al. 2006). The pathogenesis of sensory response patterns in ASD is currently not well-specified, however, disrupted attention disengagement and orienting processes may be a plausible explanation for some of the clinically observed sensory response patterns evident in children with ASD (e.g., Donkers et al., 2015).

The overlap in timing of early emerging clinical sensory responses in ASD and the emergence of attentional disengagement and orienting deficits presents further support that underlying mechanisms may be intertwined. Sensory hyporesponsiveness, hyperresponsiveness, and seeking (e.g., visual fixations) are thought to emerge in ASD in the first two years of life (e.g., Baranek 1999; Baranek et al. 2013; Ben-Sasson et al. 2008, 2009a, b; Bryson et al. 2007; Dahlgren and Gillberg 1989; Freuler et al. 2012; Osterling and

Dawson 1994; Rogers and Ozonoff 2005). Hyporesponsive behaviors are particularly associated with autism and have been reported as early as 9–12 months of age (e.g., Baranek 1999; Osterling and Dawson 1994). Sensory response patterns are reported to change with increasing age and developmental ability, but there is some disagreement on whether symptoms increase or decrease as a function of these variables (Baranek et al. 2007, 2013; Ben-Sasson et al. 2007, 2009b; Kern et al. 2007a, b; Talay-Ongan and Wood 2000). Attentional disengagement deficits also appear during this early developmental period in infant siblings who are later diagnosed with autism (e.g., Sacrey et al. 2013; Zwaigenbaum et al. 2005). “Sticky attention” was noted between 6 and 12 months (Zwaigenbaum et al. 2005), and deficits in visual attention to novel toys during play were also found at 12, 15, 18, and 24 months of age in this population (Sacrey et al. 2013). Although these studies suggest that both atypical sensory responses and disruptions in attention emerge concurrently in the first two years of life in children who are later diagnosed with ASD, more experimental research could further unravel these potential associations and underlying mechanistic explanations.

A few studies have provided evidence of a link between clinical sensory response patterns and attentional differences in preschool and school-age children with ASD. Sensory hyporesponsiveness to both social and nonsocial stimuli was found to be a significant predictor of poor joint attention (a complex social skill supported by the attentional orienting network) (Baranek et al. 2013). Another study (Liss et al., 2006) found that sensory hyperresponsiveness co-occurred with overfocused attention in almost half of their sample of children with ASD. Moreover, neural responses to auditory stimuli were found to be associated with sensory seeking behavior through complex interactions of sensory and attentional processing indices (Donkers et al. 2015). However, to our knowledge, no studies have explicitly examined the relation between attentional disengagement and orienting and clinically-derived sensory response patterns in children with ASD using an experimental gap-overlap paradigm.

The purpose of this study is: (1) to identify the specific components of attentional disengagement and orienting that are disrupted in children with ASD as compared to both typically-developing children (TD) and children with other developmental disabilities (DD) during a gap-overlap task with eye-tracking, accounting for maturational variables, (2) determine whether sensory-perceptual salience [stimulus properties: Static, Dynamic (unimodal visual), Dynamic + Auditory (multimodal visual + auditory)] of a central distractor differentially affects attentional disengagement and orienting during the gap-overlap task, and (3) determine the association between putative attentional impairments in the experimental gap-overlap task and three clinically-derived sensory response patterns (i.e., sensory hyporesponsiveness, hyperresponsiveness, and seeking) as measured with the Sensory Experiences Questionnaire, Version 3.0 (SEQ-3; Baranek 1999; Ausderau et al. 2014a, b) for children with ASD and DD.

We posited that attentional disengagement will be more impaired by both top-down and bottom-up factors for participants with ASD compared to those with DD or TD. Specifically, we hypothesized that children with ASD will have fewer and/or slower saccades to disengage from central stimuli, and fewer and/or slower saccades to reach the peripheral

stimuli relative to TD and DD peers. This deficit is hypothesized to be affected by a temporal overlap between the central and peripheral stimuli (i.e., greater impairment for the overlap condition than the baseline or gap conditions), particularly during conditions in which the perceptual salience of a central distractor is greater (i.e., more impairment for dynamic than static stimuli). For the second aim, we considered that clinical sensory response patterns may be particularly affected by attention problems. For example, inability to disengage visual attention could result in the appearance of more hyporesponsiveness if the child misses or is slow to respond to naturally occurring stimuli in the periphery, or increased seeking behaviors if the child remains stuck on a central sensory distractor. Additionally, inability to disengage attention could result in enhancement of sensory input (at the fixation point), leading to more hyperresponsive behaviors. Thus, we hypothesized that higher clinical symptoms (on SEQ-3), especially sensory hyporesponsiveness, would be associated with more impairments in attentional disengagement abilities. Finally, we considered developmental effects (age and IQ) on attention abilities across analyses.

## Methods

### Participants

Fifty children (19 ASD, 20 TD, 11 DD), ages 4–13 years participated in this study. Ten participants (1 ASD, 2 TD, 7 DD) were excluded from analyses due to equipment failure ( $N = 2$ ), behavioral challenges ( $N = 5$ ), or not meeting inclusion criteria ( $N = 3$ ).

Participants were recruited as part of a larger study using convenience sampling through university listservs, websites, diagnostic evaluation clinics, early intervention/day care programs, mental health centers, local agencies, parent support groups, and public schools. In addition, a university-based research registry was used to recruit families of children with ASD. General exclusion criteria for the study were significant vision/hearing/physical impairments, psychotic disorders and uncontrolled seizures. The experimental protocol was approved by the University's Institutional Review Board. All parents gave written informed consent, and children provided assent as possible. Families received \$20; children were given stickers and a small prize.

For children in the ASD group ( $n = 19$ ), diagnoses of Autistic Disorder (American Psychiatric Association, 2000) were determined by an independent licensed psychologist or physician, and confirmed using algorithm cutoffs on the Autism Diagnostic Interview-Revised (ADI-R) (Le Couteur et al. 2003) and Autism Diagnostic Observation Schedule-2 (ADOS-2; see Table 1) (Gotham et al. 2007; Lord et al. 2006, 2012). Children with autism were included across the continuum of IQ (both high and low functioning), as long as they could perform the tasks. We were interested in a representative sample, not limited to those with high functioning ASD. Those with known genetic conditions often co-morbid with ASD (e.g., Fragile X syndrome, tuberous sclerosis) were not recruited for this group.

The DD group was recruited as a comparison group of children with known intellectual deficits that are not associated with ASD. This group comprised 8 children with genetic syndromes associated with intellectual deficits (e.g., Down or Williams syndrome), 1 child with idiopathic developmental delay, and 2 children with a history of prematurity and

developmental delay. Inclusion criteria were overall IQ scores more than 2 standard deviations below the mean, or scores on two or more developmental domains of a cognitive assessment that were more than 1.5 standard deviations below the mean—see below for measures used. All children in the DD group were assessed to ensure they did not have clinically elevated symptoms of ASD on the ADOS-2 or Childhood Autism Rating Scale (CARS; Schopler et al. 1986), and none did.

Children in the TD group were all typically developing as confirmed by cognitive and developmental assessments (see below). They had no significant history of developmental problems, special education or intervention, and did not exhibit ASD symptoms (CARS).

### Demographic, Cognitive, and Sensory Measures

A parent-report form was used to collect demographic data (gender, race, ethnicity, socioeconomic status, etc.) to describe the sample (Table 1).

Cognitive abilities of all children were assessed with the Stanford-Binet Intelligence Scales, Fifth Edition (SB5; Roid, 2003). The SB5 was conducted as part of the larger grant project; the nonverbal score (Table 1) was retrieved from the database and used as a covariate in our analyses.

The children's clinical sensory response patterns were assessed concurrently ( $\pm 3$  months) with the eye-tracking task using the Sensory Experiences Questionnaire, Version 3.0 (SEQ-3; Baranek 1999; Ausderau et al. 2014a, b). The SEQ-3 is a 105-item questionnaire that asks caregivers to rate the frequencies of their child's behavioral responses to sensory input across modalities (e.g., visual, auditory, tactile), contexts (social, non-social), and sensory response patterns (hypo- and hyper-responsiveness, and seeking). It has been validated for children with ASD, 2–13 years (Ausderau et al. 2014a, b), and has high levels of internal consistency, test–retest reliability (Little et al. 2011), and discrimination of known diagnostic groups (Baranek et al. 2006). See Table 1.

### Eye Tracking Task

**Apparatus**—Stimuli were presented on a computer monitor (Width: 47.5 cm  $\times$  Height: 29.75 cm) with a screen resolution of 1280  $\times$  1024 pixels. Eye movements were recorded with a Tobii  $\times$  120 Eye Tracker sampled at 60 Hz (Tobii Technology, Danderyd, Sweden). Participants' faces and looking behavior were also captured with a Logitech C270 web camera positioned above the computer monitor. Two Logitech speakers were positioned to the left and right of the monitor and set at a standard volume for the auditory components of the task.

**Stimuli**—Central fixation stimuli included six novel, nonsocial objects with interesting visual and auditory qualities. The items included: (1) a multicolored globe on a vertical stick that spins and lights up when activated, (2) a neon pink and yellow slinky, (3) a multi-colored bumble ball that vibrates and moves when activated, (4) a white and pink fan with gratings that spin and make a whirring sound, (5) a tube with pink and blue water bubbles, and (6) a yellow, white, and black spiky fish that inflates after being compressed. The peripheral stimulus was a static white outline of a square. All central fixation stimuli were



captured in static and dynamic format on a black background. Items were photographed and video-recorded using a Sony Cyber-shot digital camera. The digital photographs were converted to a JPEG format using Adobe Photo Shop, Version CS4 (Adobe Systems Incorporated, San Jose, CA, USA) and the videos were converted to an AVI format using Adobe Premiere Pro, Version CS4 (Adobe Systems Incorporated, San Jose, CA, USA) software. The central stimulus measured 235 pixels wide and 228 pixels high ( $8.3^\circ \times 6.3^\circ$  visual angle), and the peripheral stimulus measured 232 pixels wide and 228 pixels high ( $8.2^\circ \times 6.3^\circ$ ). All stimuli were then entered into Tobii Studio analysis software, Version 2.2 (Tobii Technology, Danderyd, Sweden). Auditory components were added or enhanced for the videos using Adobe Premiere Pro, Version CS4 (Adobe Systems Incorporated, San Jose, CA, USA).

**Gap-Overlap Task Design**—The gap-overlap task included three conditions (Baseline, Gap, and Overlap) and three central fixation stimulus types (Static, Dynamic, and Dynamic + Auditory). All trials began with a centrally presented stimulus and remained on screen between 750 and 2000 ms. The peripheral stimulus then appeared to the left or right side of the screen in a random order at  $12.5^\circ$  eccentricity for 1250 ms (Overlap, Baseline conditions) and 1000 ms (Gap condition). Thus, complete trials (central and peripheral stimuli presented) ranged from 2000 to 3250 ms. The inter-trial stimulus, a black screen, was 500 ms. See Fig. 1 for an illustration of the task parameters and stimuli.

In the Baseline condition, the central stimulus was presented and disappeared, followed immediately (no offset-onset delay) by the peripheral stimulus to the left or right. In the Gap condition, the central stimulus was presented, followed by a blank, black screen for 250 ms, and then the peripheral stimulus. In the Overlap condition, the central stimulus was presented for the specified time and remained on the screen for the duration of the peripheral stimulus presentation.

The gap-overlap task consisted of 180 trials, comprised of 20 trials of each possible combination of condition and stimulus type (e.g., Baseline with Static stimuli, Baseline with Dynamic stimuli, etc.). The trials were presented in four blocks of 45 trials, and block order was randomly generated for each child. Each block consisted of 15 trials of each condition (Baseline, Gap, Overlap) and central stimuli were presented in all three formats (Static, Dynamic, and Dynamic + Auditory). Conditions and stimulus types were not repeated more than three consecutive times. Additionally, Tobii-generated, visual-auditory stimuli (e.g., cartoon animals that bounce and make sound) were presented at predetermined intervals several times throughout each block of trials to keep participants motivated and attending to the task.

**Procedures**—During the visit to the eye tracking lab, participants sat on a chair placed 60 cm from the computer screen in a quiet, dark room. Participants were told to “look at the pictures on the computer screen.” If a participant had difficulty remaining still, the parent or experimenter sat behind the child with eyes closed or head turned and gently held the child’s shoulders or head in place. The gap-overlap task was presented with breaks between each block of trials to allow the child to receive a sticker for their efforts and to re-focus. Children’s eyes were calibrated at the start of the eye tracking task, and were re-calibrated

after breaks between trials. One of two calibration procedures from Tobii Studio was used for each participant: regular calibration or infant calibration. Both procedures used five points, four of which were located in each corner of the screen, and one which appeared in the middle of the screen. The regular calibration includes a dot that moves to each of five points. The infant calibration includes a small animation that appears at each of the five points. The regular calibration was attempted first; however, if participants were unable to follow the directions, or attend to the moving dot, the infant calibration, which is more attention grabbing, was used.

**Eye-Tracking Data Extraction**—The eye tracking data was a direct output from the Tobii Studio, Version 2.2 (Tobii Technology, Danderyd, Sweden), “Raw Data Export” function (native.tsv format) and included all available variables and data points. Data was converted to csv format for cleaning and calculations. Tobii’s fixation detection algorithm was used to determine if participants’ eyes were looking at the screen. Visual Basic for Applications, Version 7.0 (Microsoft Corporation, Redmond, WA, USA), MatLab (The MathWorks, Inc., Natick, MA, USA), and SAS (SAS Institute, Inc., Cary, NC, USA) were used to combine all raw data, finalize cleaning and output the raw microseconds and location of gaze points to determine fixation data for analysis.

### Analytic Strategy

The first objective of this study was to evaluate between-group (ASD vs. DD vs. TD) differences in attentional disengagement from central images, presented as three stimulus types, and orienting to a peripheral target, presented under three task conditions. To be considered a valid trial initially, two criteria had to be fulfilled. First, the participant’s eyes had to be looking at the screen (as detected by Tobii). For each group, we calculated the average percent of trials (out of the total number of trials participants were exposed to) that were invalid (i.e., Tobii could not detect eyes): ASD 2.44 %, TD 1.89 %, DD 1.62 %. Significant differences between groups for this first criterion were not detected. Second, the participant’s eyes had to be fixated within the central stimulus’ defined parameters for at least 200 consecutive msec. *Central fixation accuracy* (our first outcome measure of interest) was then tallied to ensure that all groups were equally engaged in the central distractor for all three stimulus types. This measure was calculated such that successful trials are those in which participants’ eyes were fixated within the defined x/y coordinates of the central stimulus for 200 ms or more. Group differences were not detected for this outcome (see Results). Trials that did not meet both of these criteria were considered invalid and excluded from further analyses. There were four primary outcome variables to measure attentional disengagement and orienting: (1) *central disengagement accuracy* (i.e., successful trials as defined by participants’ eyes moving outside the defined x/y coordinates of the central stimulus in the correct direction of the peripheral target); (2) *peripheral saccade accuracy* (i.e., successful trials as defined by participants’ eyes reaching the defined x/y coordinates of the peripheral target); (3) *central disengagement saccade reaction time* (i.e., time for participants’ eyes to leave the defined x/y coordinates of the central fixation stimulus in the correct direction of the peripheral target); and (4) *peripheral saccade reaction time* (i.e., time for participants’ eyes to reach the defined x/y coordinates of the peripheral target). For central disengagement accuracy and peripheral saccade accuracy, trials that did not meet



these criteria were considered invalid and excluded from analyses. Reaction times were calculated only for “valid” trials as defined above.

We compared group differences separately for these outcome variables with 3-way analyses of variance (ANCOVA) for reaction time measures and logistic regression for accuracy measures with (3 groups: ASD, DD, TD  $\times$  3 central stimulus types: Static, Dynamic, Dynamic + Auditory  $\times$  3 task conditions: Baseline, Gap, Overlap) with chronological age (CA) and IQ entered as covariates. We covaried for CA and IQ because these variables may affect performance on both attention and sensory measures, and our preliminary analyses showed that the three groups differed on some of these variables—e.g., by definition the DD group had intellectual deficits whereas the typically-developing group did not. (See Table 1 for descriptives by group). Follow-up pairwise comparisons were performed with the Tukey–Kramer method. Effect sizes are estimated as Cohen’s D for main effects and sum of squares for the RT ANCOVA analyses and as parameter estimates and standard errors for the logistic regression analyses (presented in Supplementary Tables). All statistical analyses were conducted using SAS (SAS Institute, Inc., Cary, NC, USA).

The second objective of this study was to evaluate associations between attentional disengagement and orienting, and sensory response patterns, as measured by a clinical parent report, for the ASD and DD groups. We performed separate ordinary least squares regression models for three sensory response patterns (hyporesponsiveness, hyperresponsiveness, seeking) for the four main gap-overlap outcome variables (central disengagement accuracy, peripheral saccade accuracy, central disengagement reaction time, peripheral saccade reaction time). All analyses were run with CA and IQ as covariates. We combined the ASD and DD groups for this set of analyses to maximize the variability of the sensory scores and excluded the TD group from these analyses because they did not exhibit sufficient clinical sensory response patterns to provide meaningful relations to the experimental task.

## Results

### Differences in Attentional Disengagement

**Central Fixation Accuracy**—All participants had similarly high rates (ASD:  $96.5 \pm 0.3\%$ ; DD:  $95.6 \pm 0.6\%$ ; TD:  $97.0 \pm 0.5\%$ ) of successful fixation to the central stimulus at the start of each trial ( $\chi^2(2, N=50) = 2.75, p = .25$ ) (see Table 2). There were no main effects of Condition or Stimulus Type, nor any 2- or 3-way interactions ( $p > .18$  for all). There was a significant effect of IQ ( $\chi^2(1, N=50) = 10.56, p = .001$ ) such that higher IQ’s related to higher fixation accuracies. There was not a significant effect of CA ( $p = .74$ ). All means and parameter estimates are reported in Supplementary Tables.

**Central Disengagement Accuracy**—The ASD group showed impaired ability to disengage from the central fixation relative to the DD and TD groups ( $\chi^2(2, N=90) = 47.35, p < .001$ ) (see Fig. 2). Across groups, there was an effect of Condition ( $\chi^2(2, N=90) = 629.53, p < .001$ ), such that Overlap trials were less accurate than Baseline trials, which were less accurate than Gap trials. With respect to the sensory properties/salience of the central distractor, there was a main effect of Stimulus Type, such that the static stimuli were

associated with higher success at disengagement, relative to both Dynamic and Dynamic + Auditory stimuli ( $\chi^2(2, N=90) = 33.86, p < .001$ ) in all groups. There was a significant Group by Condition interaction ( $\chi^2(4, N=90) = 18.95, p < .001$ ), such that the Baseline had lower accuracy than Gap for the ASD group, but these two conditions had similar accuracies for the DD and TD groups. There was also a significant Condition by Stimulus Type interaction ( $\chi^2(4, N=90) = 38.08, p < .001$ ), such that there was only an effect of Stimulus Type within the Overlap Condition (see Fig. 3), with greater accuracy when disengaging from Static stimuli relative to both Dynamic and Dynamic + Auditory stimuli. While the Group by Stimulus Type interaction was marginal ( $\chi^2(4, N=90) = 8.52, p = .07$ ), the 3-way interaction of Group, Condition, and Stimulus Type was non-significant ( $p = .27$ ). There were also effects of CA ( $\chi^2(1, N=90) = 156.21, p < .001$ ) and IQ ( $\chi^2(1, N=90) = 47.84, p < .001$ ), such that children who are older and have higher IQ's performed better. Thus, the ASD children performed worse at disengagement than their DD and TD peers. The timing of the peripheral stimulus and the salience of the central stimulus both affected disengagement rates, as did age and IQ. All means and parameter estimates are reported in Supplementary Tables.

**Peripheral Saccade Accuracy**—The ASD group had impaired accuracy to saccade to the peripheral target relative to their DD peers ( $\chi^2(2, N=90) = 23.82, p < .001$ ), while the TD group's accuracy fell in the middle and was not significantly different (see Fig. 2). A main effect of Condition also indicated that across groups, Overlap trials were less accurate than either Baseline or Gap trials ( $\chi^2(2, N=90) = 489.26, p < .001$ ). A main effect of Stimulus Type also indicated that Static stimuli were associated with higher success at saccades to peripheral stimuli, relative to both Dynamic and Dynamic + Auditory stimuli ( $\chi^2(2, N=90) = 39.87, p < .001$ ). There was a significant interaction of Condition by Stimulus Type, with an effect of Stimulus Type only within the Overlap Condition ( $\chi^2(2, N=90) = 32.24, p < .001$ ) (see Fig. 4), such that peripheral saccade accuracy was greater when disengaging from Static stimuli compared to both Dynamic stimulus types. There were no other significant 2- or 3-way interactions ( $p > .35$  for all). There were also effects of CA ( $\chi^2(1, N=90) = 173.05, p < .001$ ) and IQ ( $\chi^2(1, N=90) = 68.21, p < .001$ ), with child age and IQ both being positively correlated with performance. Thus, ASD children performed worse at saccade to target than their DD peers. The timing of the peripheral target and the salience of the central stimulus affected saccade rates, as did age and IQ. All means and parameter estimates are reported in Supplementary Tables.

**Central Disengagement Reaction Time**—There was a main effect of Group on central disengagement reaction times ( $F(2,380) = 2.96, p = .05$ ), suggesting that all three groups were not equal, although follow-up pairwise comparisons showed no significant pairwise differences (see Fig. 2). Across groups, there was a main effect of Condition ( $F(2,380) = 9.68, p < .001$ ), such that Baseline trials had faster disengagement than Overlap trials (Cohen's  $d$ : 6.2), with Gap trials in between. Static stimuli were associated with faster disengagement than Dynamic (Cohen's  $d$ : 11.4), which had faster disengagement than Dynamic + Auditory stimuli (Cohen's  $d$ : 4.4) ( $F(2,380) = 66.19, p < .001$ ). There was a significant interaction of Condition by Stimulus Type, with an effect of Stimulus Type most predominant in the Gap Condition ( $F(4,380) = 5.74, p < .001$ ), such that disengagement

reaction time was fastest for static stimuli during the gap condition. There was also a significant interaction of Group by Stimulus Type ( $F(4,380) = 2.48, p = .04$ ), such that only the ASD group showed slower reaction times when disengaging from Dynamic + Auditory relative to Dynamic stimuli. There were no other significant 2- or 3-way interactions ( $F < 1.6$  for all). There was a significant effect of CA ( $F(1,380) = 4.31, p = .04$ ) and a marginal effect of IQ ( $F(1,380) = 3.67, p = .06$ ), such that older children and those with higher IQ's had faster disengagement reaction times. All means and sum of squares are reported in Supplementary Tables.

**Peripheral Saccade Reaction Time**—All 3 groups had similar saccade reaction times ( $F(2,370) = 2.14, p = .12$ ) (see Fig. 2). There was a main effect of Condition, such that, across groups, Baseline trials had faster saccades than either Gap or Overlap trials ( $F(2,370) = 13.12, p < .001$ ) (Cohen's  $d$ : 5.7 and 6.5, respectively). There was a main effect of Stimulus Type, such that Static stimuli were associated with faster saccades away from the central distractor than Dynamic (Cohen's  $d$ : 9.8), which were faster than Dynamic + Auditory (Cohen's  $d$ : 3.0) stimuli ( $F(2,370) = 44.75, p < .001$ ). There was a significant interaction of Condition by Stimulus Type, with an effect of Stimulus Type most predominant in the Gap Condition ( $F(4,370) = 6.71, p < .001$ ) (see Fig. 5). There were no other significant 2- or 3-way interactions ( $F < 1.7$  for all). There was no significant effect of either CA or IQ ( $F < 1.1$  for each). All means and sum of squares are reported in Supplementary Tables.

**Association of Chronological Age with Task Condition and Stimulus Type**—Because we were interested in how maturation contributes to performance, in a follow-up analysis we tested for correlations between both CA and mental age (MA) and the effect of task Condition separately for each of the three groups for central disengagement accuracy. To measure the effect of Condition, we calculated the difference between gap and overlap within the average of combined Dynamic and Dynamic + Auditory trials. For the TD group, negative correlations between both CA and MA and condition effects were found as expected—that is, as CA and MA increased, the impact of the task conditions on the accuracy of central disengagement decreased (CA:  $r = -0.51, p < .05$ ; MA:  $r = -0.47, p < .05$ ). The ASD group demonstrated a similar negative correlation with MA and condition effect for disengagement accuracy ( $r = -0.66, p < .01$ ), but no significant correlation was found with CA ( $p > .1$ ). This suggests that, as children with ASD mature mentally, there is a decrease of the impact of the task condition on the ability to disengage. No significant correlations were found between either MA or CA with condition effect for the smaller DD group ( $p > .1$  for all).

**Association of Sensory Response Patterns with Attentional Disengagement and Orienting**—Overall, all three sensory response patterns were significantly associated with attentional disengagement and orienting abilities for the children with ASD and DD combined; however, the direction of the effect differed among the sensory response patterns (see Table 3). Higher scores on hypo- and hyperresponsiveness were associated with less fixation to the central stimulus. Both elevated hyporesponsive and sensory seeking scores were associated with impaired disengagement, reflected in less successful and slower

disengagement from the central fixation stimulus. In contrast, higher hyperresponsive scores were associated with improved disengagement performance, as measured by more accurate and faster disengagement from the central fixation stimulus. Elevated symptoms across all three sensory response patterns were associated with less successful saccades to the peripheral target; however, only higher sensory seeking scores were associated with significantly slower saccades to reach the peripheral target.

Generally, higher seeking behaviors and more hyporesponsiveness were associated with poorer attentional disengagement, whereas higher levels of hyperresponsiveness facilitated attentional disengagement.

## Discussion

This study used a gap-overlap task and found evidence of disrupted attentional disengagement, reflected in less successful disengagement from a central stimulus in children with ASD relative to both DD and TD peers, controlling for age and IQ. Orienting (as reflected in saccades to peripheral targets) was also impaired in ASD relative to DD peers (who were similar on chronological age), but was comparable to chronologically younger TD children (who were similar on mental age), suggesting some evidence for maturational delays in the ASD group. As expected, disengagement from a central distractor was impacted by task condition across all groups, such that disengagement and saccades were least accurate and saccades were slowest when the central and peripheral stimuli temporally overlapped.

Several novel findings add to the literature: First, the use of highly salient perceptual stimuli (i.e., dynamic visual images with or without an auditory component vs. static) compounded the effects on disengagement and saccades during the overlap condition across all three groups. Second, the ASD group was noted to have reduced disengagement speed when presented with multimodal (audio + visual) versus unimodal (visual only) dynamic stimuli, which was not true of the other two groups of children. Third, children with ASD with lower mental ages demonstrated a greater negative impact of task condition on their ability to disengage from a central stimulus. Finally, all three clinically-derived sensory response patterns (hyporesponsiveness, hyperresponsiveness, and seeking) were significantly associated with attentional disengagement outcomes for children with ASD and DD, but in somewhat different directions. We expand on each of these findings below.

### Aberrant Attentional Disengagement and Orienting in ASD

Our findings are consistent with previous evidence of disrupted disengagement in gap-overlap paradigms in children with Autism/PDD (Landry and Bryson 2004), infants at risk for ASD (Elsabbagh et al. 2009), and at-risk infants who are later diagnosed with ASD (Elsabbagh et al. 2013). These impairments were demonstrated in this study in disengagement accuracy and saccade accuracy to peripheral targets. Because attentional disengagement and orienting are domain-general processes, disruptions in these processes may have many downstream consequences on other more specific developmental domains for children with ASD. For example, learning social-communication and language skills requires the child to notice and orient attention to social partners when they are talking and

interacting; thus, disruptions in attentional disengagement may stall development of these foundational skills, leading to a cascade of further consequences for social participation. Poor attentional control may also play a role in the development of overly-focused interests and repetitive behaviors, which are characteristic of ASD.

Previous studies have also found delayed reaction times during disengagement in children with Autism/PDD (Landry and Bryson 2004) and at-risk infants (Elsabbagh et al. 2009, 2013). Although we had a significant main effect on this variable indicating the three groups were not equal, the lack of pairwise differences are inconclusive, and require follow-up with larger samples. Adding to the literature, our study also examined peripheral saccade reaction time, which indicated that although children with ASD disengage and shift less often than control groups, when they do, saccade reaction times are comparable to controls—that is, once fixation is “unstuck,” speed is unaffected. This finding is somewhat consistent with Fischer et al. (2013), who demonstrated that high functioning children with ASD, ages 5–12 years, did not differ from typically-developing children in their saccadic reaction times to reach peripheral stimuli. However, our study suggests that disengagement differences in ASD exist, but may be at the level of ability, rather than speed, to disengage and reach a target. This pattern of results suggests that disengagement deficits in ASD are present compared to both TD and DD, but more likely result from a higher-order attentional deficit than an oculomotor deficit. Alternatively, it is possible that children with ASD benefitted from the large number of trials and normalized saccade reaction times over the course of the experiment. Both our eye tracking paradigm, and that of Fischer and colleagues, used a large number of trials (180 and 128, respectively), compared to other eye tracking paradigms (e.g., Landry and Bryson, 2004).

### Effects of Task Condition and Central Salience

This study also supports previous findings of impaired disengagement and shifting when stimuli compete for attention (i.e., temporal overlap). The overlap condition had lower disengagement and saccade accuracies relative to both the baseline and gap conditions, as well as slower disengagement and saccade reaction times for the overlap condition relative to baseline (but similar to gap). This effect was evident across all three participant groups, suggesting that temporal competition for attention affects children with ASD equivalently to their peers. For disengagement accuracy alone we found an interaction of condition and group, which reflected a facilitation effect of the gap condition for the ASD group. That is, only the ASD children had improved disengagement accuracies on the gap condition, where the central stimuli disappeared before the onset of the peripheral target, relative to the baseline condition.

Furthermore, our findings extend the literature by demonstrating a pronounced impact on disengagement when the central distractors are highly salient in their perceptual features. Although previous studies have suggested that motion processing is specifically impaired for individuals with ASD versus TD (Milne et al. 2002; Spencer et al. 2000), we found that Dynamic stimuli (relative to Static) resulted in worse disengagement and saccade accuracies and reaction times similarly across groups. Research suggests that both saccades and pursuit movements recruit the frontoparietal cortical network, including the frontal and

supplementary eye fields, the cingulate cortex, and the posterior parietal cortex (Berman et al. 1999), and thus, potentially compete for resources. It is possible that the motion of our dynamic stimuli elicited pursuit movement, demanding increased sustained attention and activating this cortical network, and thereby reduced the resources available to generate a saccade away from the central moving stimulus for all children.

Moreover, we found that although accuracy of disengagement and peripheral saccades did not differ for the unimodal (visual) dynamic versus the multimodal (visual + audio) dynamic stimuli, reaction times for successful trials were indeed longer for multimodal than unimodal dynamic stimuli. Interestingly, the ASD group showed a specific disruption in disengagement reaction time for multimodal relative to unimodal dynamic stimuli that was not apparent in either of the control groups. This novel finding suggests that auditory stimuli may be particularly salient to ASD children, or that multisensory binding is specifically deficient. Indeed multisensory integration deficits in ASD have been reported with other experimental paradigms (Foss-Feig et al. 2010; Iarocci and McDonald 2006; Magnee et al. 2011; O'Neill and Jones 1997; Russo et al. 2010). It is possible that the visual and auditory features of the multimodal stimuli in our paradigm may be processed as two independent dimensions by ASD children, thereby increasing stimulus complexity and processing load. In contrast, those features may fuse in TD children, yielding to the perception and processing of a single unitary object. This finding is also consistent with reports of increased attention to details in ASD children, at the cost of global perception processing, also reported as a “disinclination” to process the gestalt (e.g. Van Eylen et al. 2015; Koldewyn et al. 2013).

We note that for all groups, there was an interaction of task condition and stimulus type on disengagement and orienting behavior. Interestingly, for the disengagement and saccade accuracies, stimulus effects were strongest for the temporal overlap condition, demonstrating that the perceptual salience of the central stimulus was most distracting when it overlapped with the peripheral target stimulus. However, for disengagement and saccade reaction times, the perceptual salience of the central stimulus had the largest effect for the temporal gap condition (i.e. when the central stimulus disappeared before the onset of the target stimulus). This suggests that even when a central dynamic stimulus is removed from the visual field (thereby releasing overt visual attention), this temporal gap may not facilitate saccade generation, as has been reported in other studies. Given that visual information can be retained up to 500 ms (iconic memory) (Sperling 1960), the salience of dynamic stimuli could have impacted sensory memory, interfering with the expected facilitation effect of the gap condition.

### **Maturation Effects**

Our study also revealed interesting effects of maturational variables on attention such that older children and those with higher IQs, regardless of group membership, had greater rates and speed of disengagement and greater rates of peripheral saccades. Follow-up analyses further elucidated that effects of task condition were associated with both increasing chronological and mental-age for the typically-developing children, where these two variables are highly correlated. However, for the ASD group, improved performance was



only related to mental age. Between 6 and 7 years, the executive attention network improves, as reflected in faster reaction times and fewer errors during a conflict flanker task (Rueda et al. 2004). If attentional disengagement relies on frontal inhibitory control, then attentional resources may increase with age as children's frontal networks develop.

### **Associations between Clinical Sensory Response Patterns and Attentional Disengagement**

To our knowledge, this study is the first to test the association between sensory response patterns and disengagement variables on a gap-overlap task in children with ASD and DD. Our findings show that attention disengagement may be differentially affected based on severity of clinical sensory symptoms. Although several studies have found associations between the three sensory response patterns and other clinical features of ASD (e.g., Liss et al. 2006; Hilton et al. 2007), ours is one of few to demonstrate divergent patterns of association with seeking and hyporesponsiveness related to impaired performance (see Watson et al. 2011 for relationship to social-communication performance), and hyperresponsiveness related to improved performance in an experimental task.

Consistent with our hypotheses, higher hyporesponsive and seeking scores were associated with greater difficulty in both accuracy and speed of disengagement from the central stimuli, as well as less accuracy toward the peripheral targets. Higher seeking scores alone were associated with slower speed toward the peripheral targets. In contrast, hyperresponsiveness showed mixed effects such that for high hyper-responsive scores, initial fixations to central stimuli were less accurate (a similar effect was found in the hyporesponsive pattern), but once focused on the central stimulus, accuracy and speed of disengagement were improved (different from both hyporesponsive and seeking patterns). However, high hyperresponsive scores were also associated with reduced accuracy toward the peripheral targets. Thus, once fixated on the central stimuli, children with more hyporesponsive and seeking behaviors demonstrated worse disengagement, whereas children with more hyperresponsive behaviors showed improved disengagement.

These findings suggest that attentional control and sensory symptoms are intertwined and may reflect individual differences in novelty detection. Namely, children with more hyporesponsive behaviors may be less sensitive to novelty, taking longer to notice and process novel objects in their central visual field, which results in slower and less frequent disengagement and fewer saccades to the periphery. In contrast, children with higher levels of hyperresponsiveness may have higher arousal and sensitivity to subtle changes in the environment, resulting in an overwhelming experience and aversion to the perceptually-salient central stimuli. In addition, children with high levels of sensory seeking behaviors may be getting overly engaged with the central stimuli, as suggested by findings that those with higher sensory seeking disengage less often and more slowly from the central stimulus and reach the peripheral stimulus less often and more slowly. This finding is also consistent with a conceptualization of some ASD features as being linked to disproportionate local-feature-based stimulus processing. Thus, children with higher seeking responses may be over-processing local stimulus attributes, at the cost of integrating them into a global unified object percept.

Furthermore, the causal direction of these associations cannot be determined from this study. It is possible that early attentional disengagement abilities lead specifically to sensory response patterns, but it is also possible that early sensory processing deficits impact the ability to disengage and orient attention. For instance, a disproportionate attention to local attributes of stimuli and an inability to fuse those attributes into a gestalt percept may result in hyper-attentiveness to objects within the focus of attention, impacting ability to disengage. Variations across children with ASD in this overreliance to local features, or sensory binding capacity, may constitute a critical determinant of their sensory phenotypes, as well as their attentional capacity and deployment limitations. Our study is unique in that it begins to unveil associations between these varied behavioral sensory patterns, rather than clinical diagnosis, and selective cognitive mechanisms postulated to play a critical role in attention allocation.

### **Clinical Implications**

This work suggests that early intervention for young children with ASD that focuses on improving disengagement and orienting abilities may have potential for ameliorating disrupted frontoparietal systems and consequently may also improve clinical symptoms, including sensory response patterns. Intervention studies that target attentional control should consider manipulating the sensory-perceptual attributes and salience of stimuli at the center of children's attention (manipulating bottom-up, stimulus-driven attention capture circuits) as well as the timing of attention-getting stimuli in the peripheral environment to elicit disengagement and orienting of attention (targeting top-down resource allocation control circuits). Improvements in these fundamental and early-developing aspects of attention may theoretically impact several areas of deficit in ASD, including over-focused and perseverative behaviors, restricted interests, social-communicative skills, as well as sensory responses.

Interventionists should also consider the association between children's sensory response patterns and attentional control. Our findings suggest that children with higher sensory seeking behaviors and/or more severe hyporesponsiveness may benefit from peripheral stimuli that are more perceptually or socially salient than their current point of focus to engage more flexibly. Alternately, given our findings that overlapping stimuli provide increased challenges for all children, removing sources of irrelevant or over-focused attention prior to presenting new sensory or social learning opportunities may increase the "temporal gap" between stimuli, thereby facilitating disengagement and orienting. In contrast, children with high levels of hyperresponsive behaviors may benefit from environmental modifications to attenuate intense or distracting stimuli in order to improve sustained attention and engagement with more relevant or social stimuli.

### **Limitations and Future Directions**

First, examination of sensory response patterns and attentional abilities in this study was limited to one parent-report measure and one experimental task. Future studies could be enhanced with observational assessments of sensory symptoms and measures of attentional abilities in natural environments. Second, this cross-sectional study suggested that developmental variables are associated with attention disengagement and orienting.

Longitudinal studies are needed to make more definitive conclusions about maturational changes affecting performance and specific mechanisms that may be delayed in children with ASD relative to other groups. Third, sensory response patterns (as measured by the SEQ-3) are dimensional traits that may interact in children with ASD (Ausderau et al. 2014a, b); thus, future studies could address specific sensory subtypes (more homogenous subgroups of children) that might be differentially affected by impaired attentional control.

## Conclusions

This study examined the impact of sensory properties/salience of central distractors and temporal overlap on the ability to disengage and orient attention in children with ASD, relative to DD and TD peers, as well as the association between attentional impairments and clinically-derived sensory response patterns. These findings demonstrate impaired disengagement accuracy in ASD relative to DD and TD peers, and impaired orienting accuracy relative to DD peers, but comparable reaction times to disengage and reach peripheral stimuli. Further, attentional disengagement, which is poorest for all groups when central and peripheral stimuli overlap in time, is even more impaired when the central stimulus is highly salient (Dynamic versus Static). The ASD group showed poorer disengagement speed for multimodal versus unimodal dynamic stimuli. Finally, sensory response patterns in children with ASD and DD are differentially associated with attentional disengagement. Impairments in attentional control may have consequences for many areas of behavior, including aberrant sensory symptoms. Future work should consider attention disengagement and orienting as a target for treatment, as well as a possible outcome measure of efficacy.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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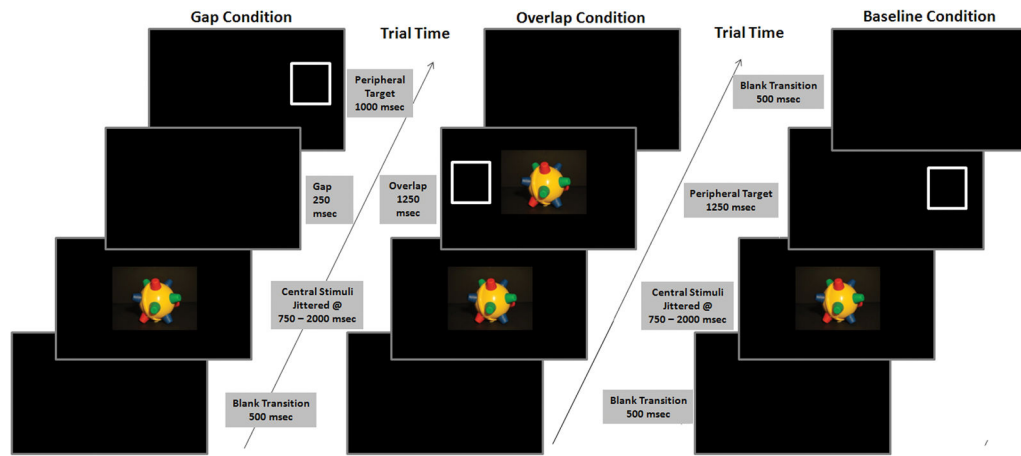
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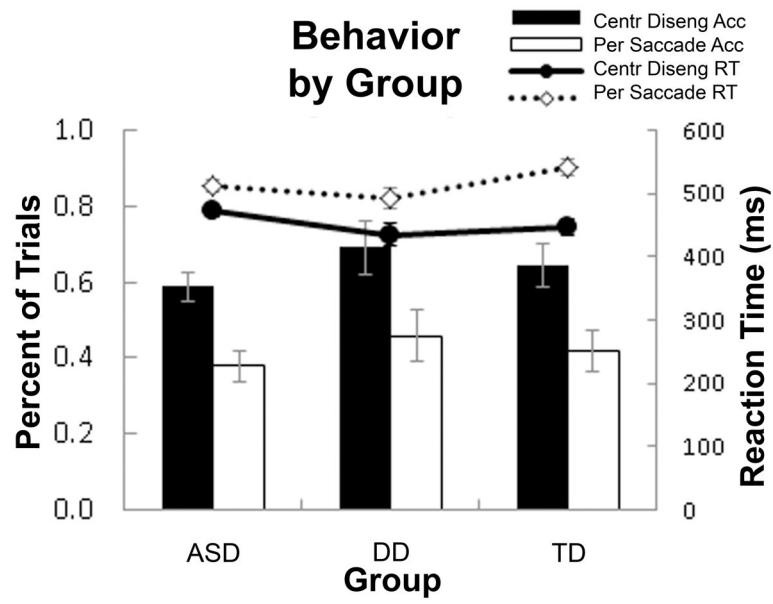
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**Fig. 1.**  
Task stimulus and design



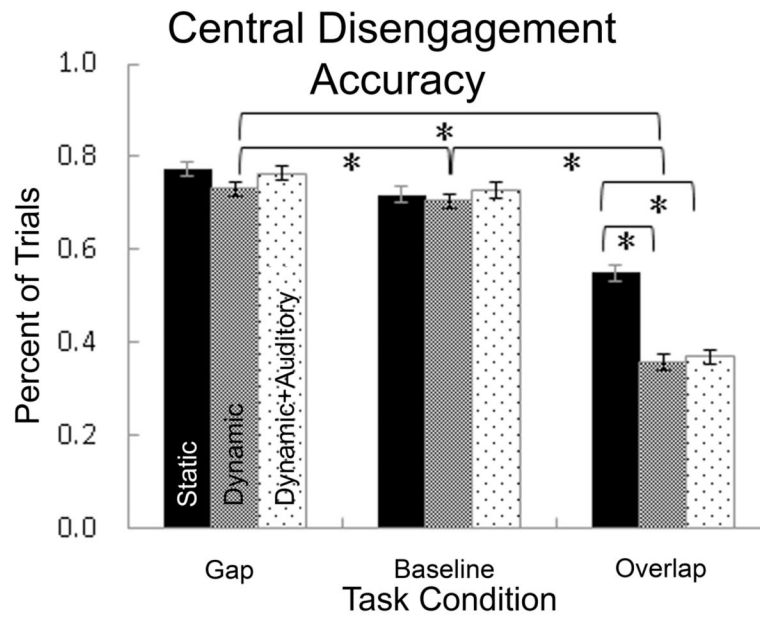
**Fig. 2.**  
Behavioral results by group

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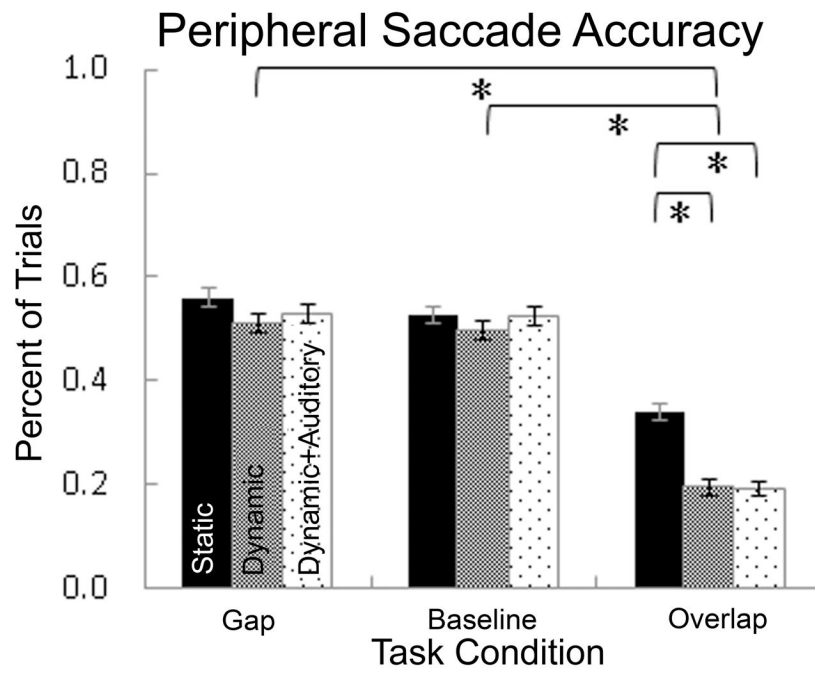
**Fig. 3.** Central disengagement accuracy by task condition and stimulus type

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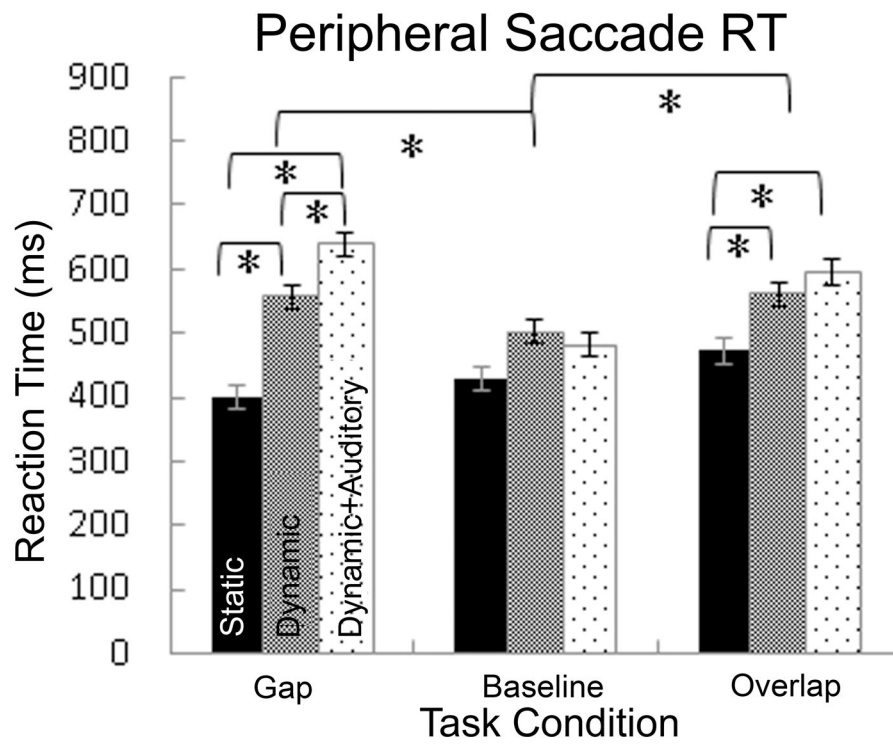
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**Fig. 4.** Peripheral saccade accuracy by task condition and stimulus type



**Fig. 5.** Peripheral saccade reaction time by task condition and stimulus type



**Table 1**

Demographics and participant characteristics

	ASD N (%)	TD N (%)	DD N (%)		
Total participants	19 (100)	20 (100)	11 (100)		
Gender (male)	15 (79)	14 (70)	6 (54.5)		
<i>Annual household income</i>					
Less than \$59,999	5 (26.3)	3 (15.0)	4 (36.4)		
\$60,000 to \$99,999	8 (42.1)	8 (40.0)	2 (18.2)		
\$100,000 or more	4 (21.1)	9 (45.0)	4 (36.4)		
Unknown	2 (10.5)	0	1 (9.1)		
<i>Race</i>					
White	17 (89.5)	17 (85.0)	11 (100.0)		
African-American, Asian, multiple races, or other	2 (10.5)	3 (15.0)	0		
	ASD M (SD)	TD M (SD)	DD M (SD)	ASD vs. TD	ASD vs. DD
ADOS severity score	8.21 (1.8)	-	1.81 (0.83)		
CARS score	30.84 (5.8)	16.73 (2.1)	21.14 (2.4)		
Chronological age (years)	8.9 (2.5)	7.0 (2.5)	10.3 (2.0)	.027	.113
Mental age (years)	7.1 (4.1)	7.9 (3.9)	4.0 (1.1)	.524	.023
IQ	79 (25)	108 (11)	54 (9)	<.001	.003
<i>SEQ</i>					
Hyporesponsiveness	2.0 (0.5)	1.3 (0.2)	1.6 (0.3)	<.001	.050
Hyperresponsiveness	2.3 (0.4)	1.6 (0.3)	2.0 (0.5)	<.001	.064
Sensory seeking	2.6 (0.5)	1.7 (0.3)	1.9 (0.5)	<.001	.002

**Table 2**

Behavioral results—central fixation accuracy

<b>Group</b>	<b>LSMEAN</b>	<b>Std Err</b>	<b>Pr &gt;  t </b>
ASD	0.965	0.101	<.001
DD	0.956	0.152	<.001
TD	0.970	0.157	<.001

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Table 3  
Association of attentional disengagement outcomes and sensory response patterns for DD + ASD (combined groups)

	Sensory	Estimate	Std Err	t Value	p
Central fixation accuracy	Hypo	-0.691	0.129	28.80	<.001
	Hyper	-0.516	0.141	13.40	<.001
	Seek	-0.114	0.133	0.73	.395
Central disengagement accuracy	Hypo	-0.242	0.065	13.67	<.001
	Hyper	0.132	0.066	3.96	.047
	Seek	-0.304	0.059	27.05	<.001
Peripheral saccade accuracy	Hypo	-0.292	0.069	18.11	<.001
	Hyper	-0.161	0.066	5.91	.015
	Seek	-0.334	0.059	32.45	<.001
Disengagement saccade RT	Hypo	0.041	0.012	3.34	.009
	Hyper	-0.039	0.012	-3.28	.001
	Seek	0.047	0.011	4.42	<.001
Peripheral saccade RT	Hypo	0.011	0.012	0.93	.355
	Hyper	-0.017	0.012	-1.50	.134
	Seek	0.037	0.010	3.64	<.001