Published in final edited form as:

J Autism Dev Disord. 2016 April ; 46(4): 1236–1246. doi:10.1007/s10803-015-2661-9.

Social-emotional inhibition of return in children with autism spectrum disorder versus typical development

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Abstract

In typical development there is a bias to orient visual attention to social information. Children with ASD do not reliably demonstrate this bias, and the role of attention orienting has not been well studied. We examined attention orienting via the inhibition of return (IOR) mechanism in a spatial cueing task using social-emotional cues; we studied 8- to 17-year-old children with ASD (n=41) and typically developing controls (TDC) (n=25). The ASD group exhibited a significantly stronger IOR effect than the TDC group, and the IOR effect correlated positively with social impairments, but was unrelated to co-occurring ADHD or anxiety symptoms. These results provide evidence of an early visual attention mechanism that is directly related to core social deficits in ASD.

Keywords

visual attention; orienting; inhibition of return; children; autism spectrum disorder; comorbidities

Introduction

Visual attention can prioritize social signals. For example, preferential looking to social stimuli is present minutes after birth, with newborns attending to upright faces relative to

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Author contributions: B.E.Y. conceived the study. B.E.Y. and V.T. programmed the experiment and generated the stimuli. M.G.M. and L.A. recruited, enrolled, and completed the experimental measures. B.E.Y. conducted or supervised almost all clinical evaluations. L.A. completed all data analyses. L.A., M.G.M., V.T., and B.E.Y contributed to manuscript preparation.

scrambled faces (Johnson, Dziurawiec, Ellis, & Morton, 1991). This preference to faces is also apparent later in life across free viewing (Klin, Jones, Schultz, Volkmar, & Cohen, 2002; Nakano et al., 2010; Rice, Moriuchi, Jones, & Klin, 2012) and various visual search tasks (Langton, Law, Burton, & Schweinberger, 2008; Riby, Brown, Jones, & Hanley, 2012; Yerys et al., 2012). Autism spectrum disorder (ASD) is characterized by social impairment, and significant evidence suggests that atypical patterns of visual attention may have positive or negative effects depending on the domain. For example, enhanced attention to visual details may lead to strengths in certain tasks, and even to developing specialized abilities (Happé, 1994; Mottron, Burack, Iarocci, Belleville, & Enns, 2003), Alternatively, reduced attention to social information may limit social learning opportunities, leading to negative downstream effects on social cognition and skill (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012; Dawson & Lewy, 1989; Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998; Keehn, Müller, & Townsend, 2013).

While multiple processes comprise visual attention, the orienting process, which allows us to disengage, shift, and reengage attention, has a strong link to how we search our environment (Posner & Petersen, 1990). Disruptions in the orienting process have consistently been found in ASD. Deficits in spontaneous shifts to faces have been observed early in life in naturalistic settings (Swettenham et al., 1998). Children with ASD and infants at high-risk for developing ASD also have difficulties disengaging their visual attention compared to controls during spatial attention tasks (Elsabbagh et al., 2009; Kikuchi et al., 2011; Landry & Bryson, 2004; Sacrey, Bryson, & Zwaigenbaum, 2013; Zwaigenbaum et al., 2005). It is not yet known if this attention impairment transcends across other facets of orienting, such as the mechanism of inhibition of return (IOR).

The mechanism of IOR reflects a bias in visual attention orienting. This orienting bias discounts previously inspected spatial locations in favor of unexplored regions and facilitates effective visual search. Disruptions to this mechanism could result in repetitive foraging of already inspected areas (Itti & Koch, 2001; Klein, 2000; Tipper, Weaver, & Watson, 1996; Wang & Klein, 2010). The IOR mechanism can be evoked and measured using a spatial cueing task in which participants are presented with a cue (e.g. picture of a face to the left or right of center) followed by a target (e.g., an asterisk ‘*’) that appears on the same (Valid) or opposite side (Invalid) of the cue’s location. When the interval between the cue and target is longer than 300 ms, individuals make a slower manual response to validly cued trials than invalidly cued trials; this difference in manual response time is known as the IOR effect (IOR effect=Valid-Invalid response time; Posner, Walker, Friedrich, & Rafal, 1984). There is evidence to support that schematic drawings of angry facial expressions diminish the IOR effect in young adults (Fox, Russo, & Dutton, 2002), and that anxiety and worry traits interact with this effect (Verkuil, Brosschot, Putman, & Thayer, 2009). Together, these findings suggest that threat-related cues are harder to disengage from and capture attention to a greater degree. Thus, using social-emotional cue stimuli in a spatial cueing paradigm provides an opportunity to test how social information may be prioritized in the orienting component of visual attention.

To our knowledge, only two small sample studies have previously examined the IOR effect in individuals with ASD, and neither used social-emotional stimuli. The first study tested the

IOR effect using a non-social cue stimulus in children with autism (without intellectual disability), Asperger's syndrome, and typically developing controls (Rinehart, Bradshaw, Moss, Brereton, & Tonge, 2008). The autism and control groups exhibited similar IOR effects, but the Asperger's syndrome group trended towards a more pronounced IOR effect compared to the control group. The second study found similar IOR effects in Asperger's syndrome and control groups (Marotta et al., 2013). These studies are likely limited by small sample sizes (*n's*<15) to detect group differences in the IOR effect. Furthermore, neither study evaluated the IOR effect using social-emotional cues with ASD; it is unknown if social-emotional cues would enhance potential group differences. Thus, it remains an open question as to whether the IOR effect is a sensitive index of altered orienting of visual attention in children with ASD.

Atypical visual attention is also observed in youth with ADHD and adults with high anxiety traits (Fox et al., 2002; Shaw, Stringaris, Nigg, & Leibenluft, 2014; Waters, Nitz, Craske, & Johnson, 2007). Symptoms of these two disorders occur frequently in individuals with ASD. For example, children with ADHD display a delayed response time and poor behavior performance in spatial cuing tasks (Ortega, López, Carrasco, Anllo-Vento, & Aboitiz, 2013), and demonstrate a trend toward a diminished IOR (Li, Chang, & Lin, 2003; White, 2007) (Li, Chang, Lin, 2002; White, 2007). For anxiety symptoms, there is a relationship between anxiety and diminished IOR in conditions with emotional face stimuli, reflecting the attentional capture of emotional faces (Fox et al. 2002, Verkuil et al. 2009, Perez-Dueñas et al, 2009, 2014). Thus, it is possible that differences in the IOR may not be related to ASD symptoms, but to the presence of these co-occurring symptoms.

We investigated the IOR effect using neutral and angry facial expressions as cues in 8–17 year-old children with ASD compared to an age-, IQ-, and sex-ratio matched typically developing cohort. Based on the prior literature, we predicted that both groups would respond slower in Valid than Invalid conditions, reflecting the IOR effect. One of the preliminary studies suggests that children with ASD may have a stronger IOR effect (Rinehart et al., 2008). Thus, we predicted a Group-by-Cue interaction where the ASD group would have a stronger IOR effect than the control group. We also hypothesized a Group-by-Cue-by-Emotion interaction, where the TDC group would have a weaker IOR effect in the angry emotion condition, but the ASD group's IOR effect would not differ between neutral and angry emotion conditions. This would reflect a deficiency in prioritizing social emotional information in children with ASD. We predicted that current ASD symptom severity would correlate with the IOR effect. There is now an appreciation for co-occurring anxiety and ADHD symptoms influencing performance on attention, executive function, and social processing tasks in youth with ASD (Corbett, Constantine, Hendren, Rocke, & Ozonoff, 2009; Herrington, Miller, Pandey, & Schultz, 2015; Hollocks et al., 2014; Pugliese et al., 2015; Sinzig, Bruning, Morsch, & Lehmkuhl, 2008; Yerys, Kenworthy, Jankowski, Strang, & Wallace, 2013). Thus, we also tested whether differences in the IOR effect are correlated with severity of co-occurring anxiety or ADHD symptoms. Predictions included that more ADHD symptoms in ASD would correlate negatively with the IOR effects overall, while more anxiety symptoms would correlate negatively with the IOR effect in the Emotional facial expression condition (emotional IOR=Angry Valid-Angry Invalid

response time), but no correlation with the IOR effect in the Neutral facial expression condition.

Method

Participants

A total of 78 children participated in the study; this included 49 ASD (without intellectual disability) and 29 TDC. The groups were matched on chronological age, sex-ratio, and General Conceptual Ability (GCA) as measured by the Differential Ability Scales – Second Edition (Elliott, 2007). See Table 1 for group characteristics. Children in the ASD group met the *DSM-IV-TR* criteria for autism, Asperger's syndrome, or pervasive developmental disorder – not otherwise specified (American Psychiatric Association, 2000), and this was confirmed with the autism diagnostic observation schedule – 2nd edition (Lord et al., 2012) and the autism diagnostic interview – revised (Lord, Rutter, & Le Couteur, 1994). Children with ASD were screened and excluded if GCA<70, if parents reported any known genetic, current mood or psychotic disorder, neurological disorder, premature birth (gestational age<37 weeks), or other significant medical condition that affects functioning. Children prescribed atypical antipsychotics were excluded, but children prescribed stimulant medication were asked to withhold on the day of the study (n=6). TDC participants were screened and excluded if parents reported any known genetic, language, learning, neurological, or psychiatric disorder, premature birth, or first- or second-degree relative with ASD. TDC children were also excluded if parents reported elevated symptoms on the Child and Adolescent Symptom Inventory (CASI-4R; Gadow & Sprafkin, 2000, 2010) or ADHD Rating Scale (DuPaul, Power, Anastopoulos, & Reid, 2016). Three TDC participants were excluded for the following: significant sleep disturbances (n=1), premature birth (n=1), and computer error (n=1). Five ASD participants were excluded for the following: GCA standard score below 70 (n=1), congenital visual problems (n=2), brain abnormality (n=1), and computer error (n=1). Four additional children were dropped after completing the task (see Data Processing and Analysis Plan)

As shown in Table 1, there were no differences in age, sex-ratio or GCA standard score across groups; the ASD group had higher ADHD rating scale scores than TDCs.

Stimulus and Materials

The **Social-Emotional Inhibition of Return (IOR) Task** displayed stimuli on two white rectangular boxes to the left and right of the center of the screen over a light gray background, on a 17-inch laptop using E-Prime version 2.0 (Psychology Software Tools Inc., Pittsburg, PA). Seven female and six male actors were used from the NimStim photoset (Tottenham et al., 2009) to create 20 neutral and 20 angry cues. The cues included open and closed mouths for both emotions. Disparities in numbers between male and female actors were a result from matching sex and ethnicity in each emotion condition. This was done to prevent sex or ethnicity biases toward one emotion condition.

Participants were seated approximately 50 cm from the laptop and were instructed to keep their eyes on the plus sign in the middle of the screen and press the corresponding 'L' or 'R'

labeled key on the side the red “star” (i.e. asterisk ‘*’) appeared as quickly and as accurately as possible. They were also told that other images would appear on either side, but would not be predictive of where the red star appears.

The IOR task was adapted from Fox, Russo, & Dutton, (2002). The task consisted of 200 trials divided into 4 blocks. The first two blocks included only neutral faces and the last two blocks included only angry faces. This was done to minimize potential cumulative effects of viewing angry faces (Compton et al., 2003; Dalgleish, 1995; Herrington et al., 2005; Holle, Neely, & Heimberg, 1997; Koven, Heller, Banich, & Miller, 2003). Participants were presented with a screen that stated ‘Hit the spacebar when you are ready to begin’ in the beginning of each block. This was done so that they could take a self-paced break in between blocks. Each trial began with a fixation cross for 200 ms. A face cue was presented in one of the peripheral boxes for 300 ms, blank peripheral boxes were presented for 200 ms, followed by 300 ms of a darkened fixation cross. The initial fixation was presented for 160 ms, followed by the red asterisk target in the upper half of the right or left white box until the child responded or 2000 ms elapsed. Each block ended with 1000 ms of a fixation cross. The cue-target onset asynchrony was a total of 960 ms and the intertrial interval was 1000 ms.

The IOR task consisted of three types of trials. See Figure 1. Of the 200 total trials, 160 consisted of target trials which varied in the facial expression and side of the cue stimulus; half of these target trials were Valid, in which the cue and target appeared on the same side, and the other half were Invalid, where the cue and target appeared on opposite sides. Forty catch trials were included; twenty were right-side cues without a target asterisk, and twenty were left-side cues without a target asterisk and were interspersed through the blocks. The catch trials were included to ‘catch’ children with a bias to responding impulsively without attending to the task.

The **Autism Diagnostic Observation Schedule-2 (ADOS-2)** is a semi-structured, standardized diagnostic measure designed to assess the domains of Social Affect, and Restricted and Repetitive Behaviors (Lord et al., 2012). Clinicians observe and code these behaviors, which are converted into algorithm scores for each domain. Each domain raw score and the combined raw score total can be converted into a Calibrated Comparison Score that takes age into account for the Module. Scores range from 1–10, and higher scores indicate greater severity (Gotham, Pickles, & Lord, 2009; Hus, Gotham, & Lord, 2012; Hus & Lord, 2014). The present study used the raw scores for Social Affect as an individual domain and the overall Calibrated Comparison Score that combines Social Affect and Restricted Repetitive Behaviors.

The **ADHD Rating Scale IV** (DuPaul et al., 2016) screens for severity in inattention and hyperactivity/impulsivity symptoms. This 18-question scale yields two domains: inattention and hyperactivity/impulsivity. For each question, parents use a 0–3 scale to rate the participant. A higher score indicates greater symptom severity.

The **Child and Adolescent Symptom Inventory-Fourth Edition Revised** is a 142-item questionnaire that screens for childhood psychopathology in children ages 5 to 18. For the

purposes of the present study, we used a subset of the Anxiety scale – the CASI 20 - developed by Sukhodolsky and colleagues (2008) to reduce measurement confounding when assessing anxiety in the presence of ASD. All individual items are scored on a scale of 0–3, with higher scores indicating greater symptom severity.

Procedures

This study was conducted at the Center for Autism Research at The Children's Hospital of Philadelphia. All participants and their guardians completed a battery of tests examining the neuropsychological, neural, and genetic basis of cognitive control in ASD. If participants were re-recruited from prior studies within one year, diagnostic and cognitive tests were not readministered. The hospital's Institutional Review Board approved the research protocol. Prior to participation, consent was obtained from all legal guardians and assent was obtained from all children. Parents completed the ADHD Rating Scale and Child and Adolescent Symptom Inventory either prior to the visit or the same day.

Data Processing and Analysis Plan

Accuracy and response time (RT) for accurate trials were calculated for each participant. Outlier trials were defined within each participant as an RT of two standard deviations above or below their mean; RTs defined as outliers were dropped from RT analyses, but correct outlier trials were still counted in accuracy analyses. After dropping outlier trials, we calculated the accuracy and average RT for each trial type (i.e. Neutral Valid, Neutral Invalid, Angry Valid, Angry Invalid) and percentage of catch trial errors. Additionally, we dropped one participant in the TDC group that had an average RT two standard deviations from the group mean, two participants in the ASD group that had an overall accuracy of <50%, and one participant in the ASD group with >50% Catch trial errors. Thus, after removing children who met exclusion criteria described above and those whose task performance were significant outliers the final sample included 41 children in the ASD group, and 25 in the TDC group.

A 2 (Cue: Valid, Invalid) × 2 (Emotion: Neutral, Angry) × 2 (Group: TDC, ASD) repeated measures ANOVA was used. Effect sizes are reported with *p*-values for significant main effects and interactions in ANOVAs (*eta* squared, η^2), and Welch's t-tests (Cohen's *d*). The directionality of interaction effects revealed by the omnibus ANOVA (*F*) is determined with an independent Welch's t-test (unequal variance). We also conducted a Pearson's *r* correlation to examine the relationships between the IOR effect and the ADHD rating scale, and CASI 20, and a Spearman's *rho* correlation to examine relationships between the IOR effect and ADOS-2 (Sears et al., 1999).

Results

Accuracy

There was no main effect of Group for accuracy, $F(1, 64)=2.07$, $p=0.16$, $\eta^2=0.01$. There were no main effects for Emotion, $F(1, 64)=0.89$, $p=0.35$, $\eta^2<0.01$, or Cue, $F(1, 64)=0.06$, $p=0.81$, $\eta^2<0.001$. There were no significant interactions (all Fs<2.35, all ps>0.12, all

η^2<0.01). There was a significant difference in catch trial errors between groups, t(47.94)=362, p<0.001, d=0.74, with the ASD group exhibiting more errors.

Response Time (RT)

There was no significant main effect of Group, F(1, 64)=0.79, p=0.38, η^2=0.01, or Emotion, F(1, 64)=0.54, p=0.47, η^2<0.001 (See Table 2 for RT means). There was a significant main effect of Cue, F(1, 64)=69.82, p<0.001, η^2=0.02, with faster RT in Invalid trials than in Valid trials, reflecting the IOR effect. There was a significant Group-by-Cue interaction for RT, F(1, 64)=5.74, p=0.02, η^2<0.01 (See Figure 2). There was no significant group difference for Valid trials, t(59.84)=1.3, p=0.19, d=0.32, or Invalid trials, t(56.86)=0.54, p=0.59, d=0.13. No other interactions were significant (all Fs<1.14, all ps>0.29, all η^2<0.001). To follow up the Group-by-Cue interaction, we ran an independent samples t-test for an Overall IOR effect which collapsed emotion conditions (([Angry Valid RT − Angry Invalid RT] + [Neutral Valid RT − Neutral Invalid RT])/2), t(51.70)=2.41, p=0.02, d=0.61.

Correlations with Overall and Emotional IOR

Within the ASD group, the Overall IOR correlated positively with the ADOS-2 Social Affect (*rho*=0.36, p=0.02), and ADOS-2 Total Calibrated Comparison score (*rho*=0.40, p=0.01; Figure 3). However, within ASD and TDC groups there was no significant relationship between the Overall IOR effect and the total raw score from the ADHD Rating Scale (all rs<0.16, all ps>0.32) or the CASI 20 anxiety scale (all rs<0.13, all ps>0.55). Taken together, these correlations suggest the stronger IOR effect is related to ASD symptoms (notably social), but is not significantly related to co-occurring anxiety or ADHD symptoms. Contradictory to our hypotheses, symptoms of anxiety were not related to the emotional IOR in either group (all rs<0.13, all ps>0.45).

Follow-Up Analysis

We observed a significant difference in Catch trial performance, documenting the large response bias in the ASD group (d=0.74). Because the IOR effect may be influenced by a response bias, we ran additional analyses to evaluate whether performance difference on Catch trials played a role in the significant difference between groups in Overall IOR. Groups were significantly different in number of participants with catch errors, X^2(1, N = 66) = 9.48, p<0.01, therefore we dropped all participants who made these errors (TDC=2; ASD=18), leaving a sample of 23 TDC and 23 ASD participants.

In this sample we found no main effects or interactions for accuracy (all Fs<0.80, all ps>0.37, all η^2<0.01). Consistent with the original analysis, we found a similar pattern of results in RT with no main effect of group, F(1, 44)=0.02, p=0.88, η^2<0.001, a significant main effect of cue, F(1, 44)=57.37, p<0.001, η^2=0.02, and a significant group-by-cue interaction, F(1, 44)=8.49, p<0.01, η^2<0.01. There were no other significant effects or interactions (all Fs<0.52, all ps>0.47, all η^2<0.001). Overall IOR continued to be significantly different between groups, t(43.59)=−2.91, p<0.01, d=0.87, and correlated with Social Affect symptoms (*rho*=0.43, p=0.04), and calibrated severity (*rho*=0.46, p=0.03).

Discussion

The present study demonstrated that the orienting component of visual attention is disrupted in ASD. Both groups responded faster to the Invalid trials than the Valid trials, reflecting the IOR effect; however, the ASD group was less accurate and had a stronger IOR effect than the TDC group. The IOR effect in the ASD group was positively correlated with social affect and total ASD symptom severity, but was not significantly correlated with ADHD or anxiety symptoms. Thus, this study identified an early mechanism of attention that contributes to atypical attention in ASD, and is associated with core social deficits but not common co-occurring symptoms.

Although the TDC group was predicted to demonstrate a reduced IOR effect for angry facial expressions relative to neutral facial expressions, this effect was not observed. This lack of difference between emotional expressions fails to replicate a prior study in young adults using a similar emotional spatial cueing task (Fox et al., 2002). These discrepant findings may be accounted for by differences in the methodology and samples, which are outlined below.

First, Fox and colleagues (2002) used schematic drawings of faces while the present study used photographs of social-emotional faces. The use of real photographs regardless of facial expression may have captured visual attention to a greater degree across all trial types than schematic faces, diminishing the valence effect (i.e. angry > neutral). Our observation that the TDC group had a weaker IOR effect than what has been observed previously (Fillmore, Milich, & Lorch, 2009; MacPherson, Klein, & Moore, 2003; Marotta et al., 2013; Rinehart et al., 2008), is consistent with this argument.

Secondly, the present study's paradigm blocked the emotion conditions rather than interspersing them. As noted above, this choice limited potential 'bleeding' effect of the anger expression condition into the neutral expression condition, but it may have also led to the TDC participants to habituate to the emotional stimuli.

Third, there are differences between samples in the present and prior study. The present study's TDC group included youth, whereas the prior investigation included college age students. There may be developmental differences in how emotional stimuli influence the IOR effect. Also, the present study's TDC group inclusion criteria required no significant psychopathology, and this may have limited variability in their anxiety (See Table 1), which would have contributed to null findings in the present study's Emotion conditions. This point is supported by a recent study showing that young adults with both high-trait anxiety *and* worry demonstrated a weakened IOR effect with emotional stimuli (Verkuil et al., 2009).

The present study extends the field's knowledge by identifying an early stage of attention (orienting) as altered in children with ASD, and by linking impaired orienting with social impairments in ASD. This study's key findings provide empirical support for Keehn et al.'s (2013) hypothesis that early attention processes contribute to core ASD symptoms. While studies have demonstrated altered development of attention orienting in children with ASD and infants at high-risk to develop ASD (Elison et al., 2013; Elsabbagh et al., 2009; Keehn, Lincoln, Müller, & Townsend, 2010), none have demonstrated a linear relationship between

orienting of attention and social impairments. The present study's large sample size may have led to the observation of this relationship. Moreover, other social motivation hypotheses of ASD have argued that visual attention prioritizes social signals and these hypotheses would also predict that altered attention orienting would be one potential process to have a cascading effect on social development (Chevallier et al., 2012; Geraldine Dawson, Webb, & McPartland, 2005; Schultz, 2005). While the findings from the present study cannot distinguish between a domain general impairment in attention orienting and a specific impairment for orienting attention with social information, the present study lays the groundwork for future investigations in this area.

Prior studies of the IOR effect in children with ASD using flashing boxes as peripheral cues found similar effects across ASD and control groups (Marotta et al., 2013; Rinehart et al., 2008). The use of non-social cue stimuli, as well as the small sample size (n's<15 per group) may have limited their ability to detect group differences. Despite the small sample sizes, one study reported trends of a stronger IOR effect in an Asperger's syndrome subset (Rinehart et al., 2008). The present study revealed significant group differences in the IOR effect, likely because the present study's sample size was nearly three times larger than prior studies, and because the present study used pictorial social-emotional cues. While speculative, the pictorial stimuli may have captured attention in both groups to a greater degree and led to larger suppression/inhibition in the ASD group, which in turn led to the larger IOR effect. This speculation is consistent with the hypothesis that children with ASD do not prioritize social stimuli to the same degree as TDC children (Chevallier et al., 2012; Dawson et al., 2005; Dichter et al., 2010; Kohls, Chevallier, Troiani, & Schultz, 2012).

Interestingly, previous work has demonstrated that children with Asperger's syndrome display a weaker IOR effect when the spatial cueing task placed faces in the center of the screen and used eye gaze to direct attention to the periphery (Marotta et al., 2013). Comparing this finding to the present study is difficult, because the present study's paradigm did not require children to make explicit use of social information. Furthermore, cues at the center of the screen that direct attention to another location (endogenous cues) are known to influence visual attention differently than peripheral cues that are drawing visual attention to a specific location (exogenous cues; Lupiáñez et al., 2004). In future studies, it may be useful to independently manipulate implicit and explicit processing of social-emotional information, as well as endogenous and exogenous cueing to examine how these factors influence orienting of visual attention in ASD.

The positive correlation between the stronger IOR effect and ASD symptoms, but not anxiety or ADHD symptoms, demonstrates that the orienting process of visual attention may be specific to ASD deficits. Indeed, if ADHD or anxiety symptoms were influencing the task performance, we would also have observed an overall diminished IOR effect or an interaction with Emotion condition, respectively. These effects were not observed in the overall ANOVA. Therefore, it is unlikely that the results can be explained by these co-occurring symptoms.

Future research can expand on the present findings in several ways. First, it is important to tease apart whether the stronger IOR effect in the ASD group and its relationship to ASD

symptoms are specific to social-emotional peripheral cues. If the IOR effect correlates with ASD symptoms when non-social emotional stimuli are used as peripheral cues, then this would suggest that the orienting component of visual attention is generally disturbed in ASD. Interventions targeting improved orienting of visual attention could support individuals with ASD. Such interventions have already been piloted in healthy toddlers (Wass, Porayska-Pomsta, & Johnson, 2011). If the effect is specific to social-emotional stimuli, then this is compatible with a burgeoning field of research to improve attention to social-emotional information in ASD (Clark-Elford et al., 2015; Tanaka et al., 2010).

Second, normative studies have demonstrated that the IOR effect has strong connections to visual search ability. Larger IOR effects are thought to support enhanced visual search capabilities. Thus, this enhanced IOR effect may be one mechanism to support the putative enhanced visual search capabilities in ASD (Jolliffe & Baron-Cohen, 1997; Kaldy, Kraper, Carter, & Blaser, 2011; O'Riordan, Plaisted, Driver, & Baron-Cohen, 2001; Rutherford, Richards, Moldes, & Sekuler, 2007). Future studies should confirm this finding in ASD by pairing spatial cueing tasks with visual search paradigms.

Third, future studies should examine the time course of both IOR and facilitation effects using manual and saccadic responses in individuals with ASD. These two effects unfold over different time courses (Briand, Larrison, & Sereno, 2000), and initial evidence suggests that the IOR effects may be similar in magnitude, but have an earlier time course in adults with ASD versus controls (Pieron, Seassau, Leboyer, & Zalla, 2014). The present study only examined one cue-target onset asynchrony that could elicit the IOR effect, similar to paradigms used in prior studies (Fox et al., 2002; Marotta et al., 2013; Rinehart et al., 2008). Thus, future investigations may examine whether the present finding of a stronger IOR effect in ASD is influenced by the cue-target onset asynchrony, as well as the potential role of response format. Furthermore, it will be important to dissociate the effects of exogenous vs. endogenous attention at the mechanistic level, which support distinct underlying attentional processes. For example, exogenous attentional orienting has been linked to programming of unexecuted eye movements whereas endogenous attention is thought to reflect top-down preparation in order to maintain goal-directed behavior. Because these two systems rely on partially distinct, yet interacting neural substrates (Chica, Bartolomeo, & Lupiáñez, 2013; Pinto, van der Leij, Sligte, Lamme, & Scholte, 2013), future work examining these differences may lead to the more precise neural link underlying visual attention deficits in ASD.

Finally, the lack of a correlation between the IOR effect and co-occurring anxiety and ADHD symptoms suggests this alteration in visual attention may be specific to ASD. The lack of a relationship between anxiety and Overall IOR effect converges with recent findings that co-occurring anxiety symptoms has little influence on attention vis à vis attentional biases in ASD (Hollocks, Ozsivadjian, Matthews, Howlin, & Simonoff, 2013; May, Cornish, & Rinehart, 2015). Furthermore, the lack of a correlation between the Overall IOR effect with ADHD symptoms in the present study aligns with a prior study showing no differences among ASD and ADHD groups' orienting during the complex attentional network task (Samyn, Roeyers, Bijttebier, & Wiersema, 2013). Thus, the potential specificity of this finding to ASD should be followed up in future investigations. Reliability of the stronger

IOR effect with social-emotional cues in ASD, and relationship to ASD symptoms require replication. If these findings are replicated and reliability is established, then future research may explore measuring the IOR effect in children at high-risk for an ASD to predict diagnosis.

It is important to note that the present study only included children with ASD without intellectual disability. Therefore, it is imperative to replicate this study in individuals with intellectual disabilities to confirm whether the pronounced IOR effect and its relationship to social impairment are present across the cognitive spectrum.

Conclusion

In summary, when using social-emotional cues, the ASD group had a significantly stronger IOR effect compared to the TDC group. This pronounced IOR effect did not correlate with ADHD or anxiety symptoms, but did correlate with measures of social affect and severity in the ASD group. These findings suggest that this attention impairment may be specific to ASD. The pronounced IOR effect in the ASD group indicates greater deficits in orienting visual attention in the context of social-emotional stimuli. This finding is in line with hypotheses regarding deficits in early visual attention mechanisms having a cascading effect on atypical social development in ASD.

Acknowledgments

We thank the many children and families for their participation in the study. The study was sponsored by grants from the National Institute of Mental Health (K23MH086111; PI: B.E. Yerys, R21MH092615; PI: B.E. Yerys, RC1MH088791; R.T. Schultz), and a New Program Development Award to B.E. Yerys through the Intellectual and Developmental Disabilities Research Center funded by the National Institute of Child and Human Development (P30HD026979; PI: M. Yudkoff), a grant from the Philadelphia Foundation, a grant from the Pennsylvania Department of Health (SAP #4100042728) to R.T. Schultz, a grant from the Pennsylvania Department of Health (SAP # 4100047863) to R.T. Schultz, a grant from Pfizer to R.T. Schultz, and a grant from the Robert Wood Johnson Foundation, #6672 to R.T. Schultz.

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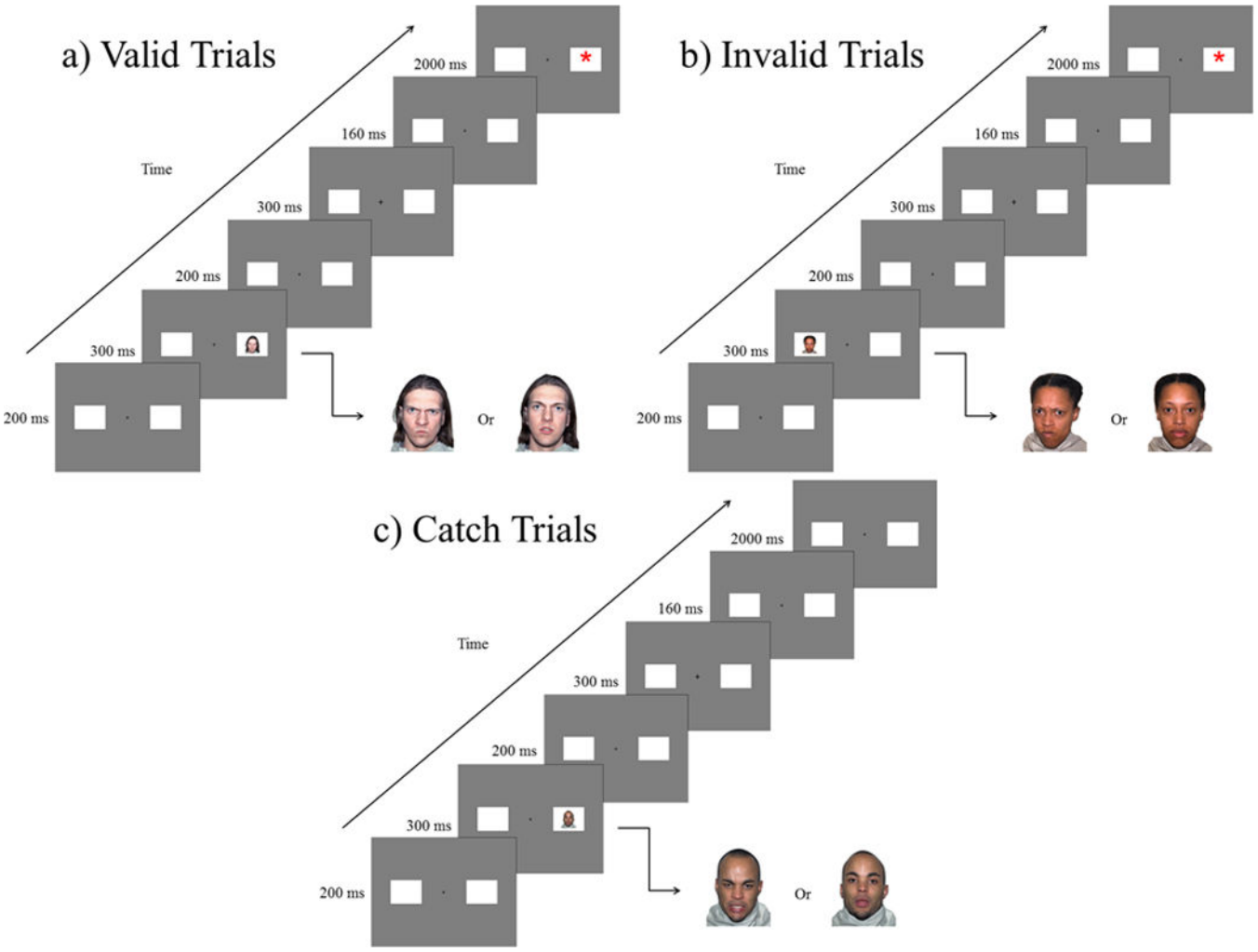

Figure 1.

The IOR task. a) Valid trials in which the cue and the target were presented on the same side. b) Invalid trials in which the cue and target were presented on opposite sides. c) Catch trials where no target was presented after a cue.

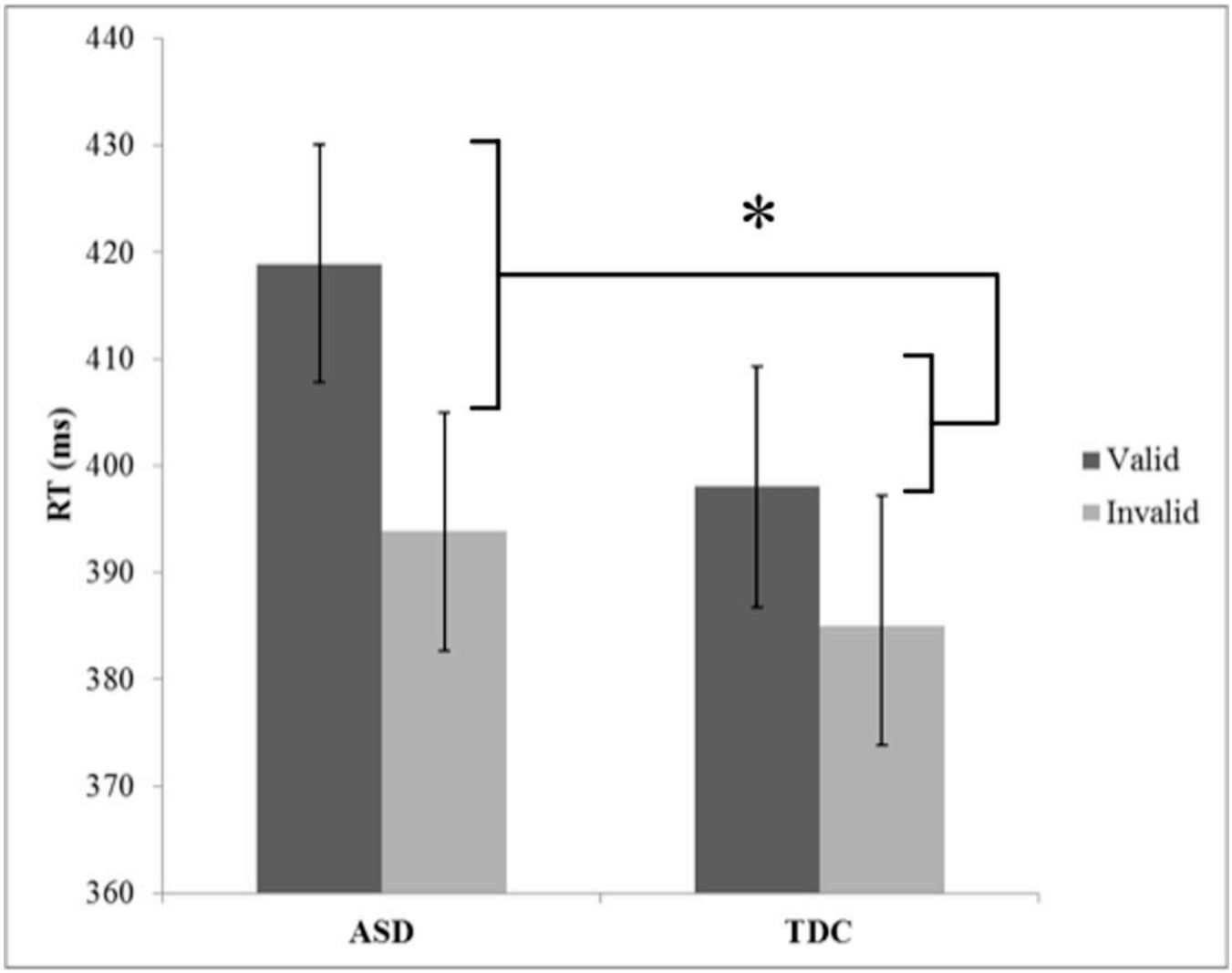

Figure 2.
Bar graph displaying the post-hoc analysis for Group-by-Cue interaction.

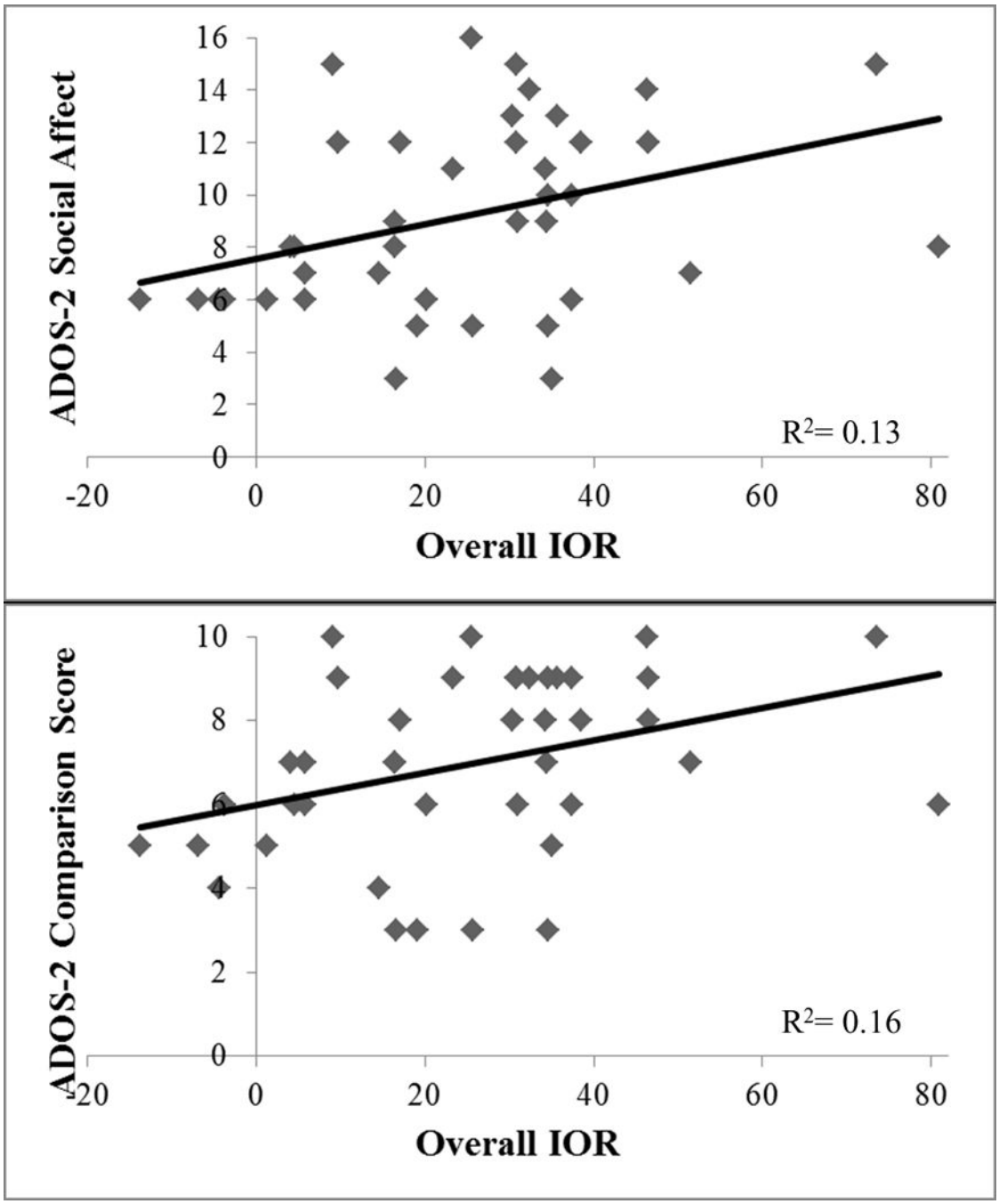

Figure 3.
Correlation between Overall IOR effect and ADOS-2 scores. Top graph displays ADOS-2 Social Affect raw score.

Table 1

Participant characteristics by diagnostic group.

	TDC n=25	ASD n=41	*p*-value
Age (years) *M*(SD)	13.27 (2.26)	12.73 (2.30)	0.35
Range	10.08–17.17	8.17–17.58	
GCA (SS) *M*(SD)	110.44 (17.26)	106.10 (17.91)	0.33
Range	92–149	79–154	
Sex (M:F)	19:6	33:8	0.67
ADI Soc. *	--	19.18 (5.14)	--
Range		3–27	
ADI Verbal Comm. *	--	15.20 (4.34)	--
Range		6–24	
ADI RRB *	--	6.23 (1.97)	--
Range		3–10	
ADOS-2 Social Affect	--	9.22 (3.57)	--
Range		3–16	
ADOS-2 RRB	--	2.76 (1.59)	--
Range		0–6	
ADOS-2 CCS	--	6.95 (3.25)	--
Range		3–10	
ADHD Total Raw	3.48 (3.24)	21.44 (10.41)	<0.001
Range	0–11	5–45	
CASI Anxiety Raw	1.88 (2.15)	10.95 (7.26)	<0.001
Range	0–7	0–32	

CCS=Calibrated Comparison Score
GCA=Global Composite Ability
RRB=Restricted and Repetitive Behaviors
SS=Standard Score (*M*=100; SD=15)

* n=40

Table 2

Task performance by diagnostic group

	TDC *M* (SD)	ASD *M* (SD)
Neutral-Valid		
Accuracy (%)	98.40 (2.38)	97.87 (2.66)
RT (ms)	398 (56)	415 (71)
Neutral-Invalid		
Accuracy (%)	99.10 (1.59)	97.80 (2.92)
RT (ms)	387 (56)	392 (67)
Anger-Valid		
Accuracy (%)	98.20 (3.50)	98.60 (1.86)
RT (ms)	398 (59)	423 (76)
Anger-Invalid		
Accuracy (%)	98.90 (2.05)	98.05 (2.34)
RT (ms)	384 (68)	396 (81)
Catch Trial Errors		
Errors (%)	**0.20 (0.69)**	**1.83 (2.74)**
Overall		
Accuracy (%)	98.65 (1.58)	98.08 (1.55)
RT (ms)	392 (58)	406 (70)
Overall Valid		
RT(ms)	398 (56)	419 (71)
Overall Invalid		
RT(ms)	385 (61)	394 (71)
Overall IOR		
RT (ms)	**12.97 (19.66)**	**25.08 (20.08)**

Note: Bold variables indicate significant difference between groups ($p<0.05$)