
Downloaded from:

Usage Guidelines:
Please refer to usage guidelines at contact lib-eprints@bbk.ac.uk. or alternatively
Visual search and autism symptoms:

What young children search for and co-occurring ADHD matter

Doherty, B.¹, Charman, T.³, Johnson, M. H.², Scerif, G.¹⁺, Gliga, T.²⁺ and The BASIS Team*

+ joint last authors


Affiliations: 1) Department of Experimental Psychology, University of Oxford, UK
2) Centre for Brain and Cognitive Development, Birkbeck College, University of London, UK; 3) Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK; 4) Autism Research Centre, University of Cambridge, Cambridge, UK; 5) Department of Psychiatry, McGill University;

Corresponding author: GS

E-mail: gaia.scerif@psy.ox.ac.uk
Highlights

• Superior visual search characterises autism spectrum disorder (ASD)
• 3-year-olds at familial risk for ASD searched for multiple perceptually or categorically defined targets
• ASD symptom severity was associated with poorer categorical search, rather than overall enhanced performance
• ASD and ADHD symptoms were both associated with more disorganized search paths
• ASD traits do not always convey an advantage in visual search
Abstract

Superior visual search is one of the most common findings in the autism spectrum disorder (ASD) literature. Here, we ascertain how generalizable these findings are across task and participant characteristics, in light of recent replication failures. We tested 106 3-year-old children at familial risk for ASD, a sample that presents high ASD and ADHD symptoms and 25 control participants, in three multi-target search conditions: easy exemplar search (look for cats amongst artefacts), difficult exemplar search (look for dogs amongst chairs/tables perceptually similar to dogs), and categorical search (look for animals amongst artefacts). Performance was related to dimensional measures of ASD and ADHD, in agreement with current research domain criteria (RDoC). We found that ASD symptom severity did not associate with enhanced performance in search, but did associate with poorer categorical search in particular, consistent with literature describing impairments in categorical knowledge in ASD. Furthermore, ASD and ADHD symptoms were both associated with more disorganized search paths across all conditions. Thus, ASD traits do not always convey an advantage in visual search; on the contrary, ASD traits may be associated with difficulties in search depending upon the nature of the stimuli (e.g., exemplar vs. categorical search) and the presence of co-occurring symptoms.
Introduction

Enhanced visual search ability is one of the most consistent findings in the autism spectrum disorder (ASD) literature. Beginning with the seminal paper by Plaisted, O’Riordan, and Baron-Cohen (1998), superior visual search has been documented in ASD from toddlerhood (Blaser, Eglington, Carter, & Kaldy, 2014; Kaldy, Giserman, Carter, & Blaser, 2016; Kaldy, Kraper, Carter, & Blaser, 2011). Superior visual search during infancy was shown to predict the severity of later ASD symptoms and ASD clinical diagnosis (Cheung et al., 2016; Gliga, Bedford, Charman, Johnson, BASIS Team, 2015a). However, superiority in visual search is not always replicated, with variation in task design potentially explaining some inconsistency in findings. With regard to task design, previous publications demonstrate that the nature of the target/distractor differences will affect whether participants with ASD show superiority in visual search. For example, superior search is observed more often when target and distractor are perceptually similar (e.g. Duncan & Humphreys, 1989; Plaisted, O’Riordan, & Baron-Cohen, 1998), but not when perceptual load is too high (e.g. Hessels, Hooge, Snijders, & Kemner, 2014). Based on what we know about the phenotypic profile of ASD, one can make further predictions about when search would put them at an advantage or disadvantage. Given the evidence for difficulties with making inferences based on category knowledge in ASD (see Naigles, Kelley, Troyb, & Fein, 2013 for thorough discussion), it is possible that difficulties with searching for targets belonging to a superordinate category (e.g. “animals”) as opposed to a basic category (e.g. “a cat”), will be exacerbated in participants with this disorder. Previous research in neurotypical individuals suggests that searching for a superordinate category (“footwear”) as opposed to a basic category (“boots”) proves generally more difficult (Maxfield & Zelinsky, 2012; Schmidt & Zelinsky, 2009). This is probably due to the lack of specificity that helps to guide visual search to realistic, complex objects; the longer time required to verify that the target is a
member of the superordinate category; and the tendency to combine instances of a category into a prototype that has little overlap with specific search target exemplars (Hout & Goldinger, 2015; Yang & Zelinsky, 2009; Zhang, Yang, & Samaras, 2006). Neural measures also indicate that search guided by categorical attentional templates is not as efficient as item-specific search (Wu et al., 2013). These difficulties might be further exacerbated in ASD but have been little investigated. Although in most real life situations search will be guided by both low-level perceptual characteristics of searched-for items (Duncan & Humphreys, 1989; Treisman, 1991), but also their higher-level categorical characteristics (Maxfield & Zelinsky, 2012; Schmidt & Zelinsky, 2009), the majority of the visual search literature in ASD to date has used targets and distractors with poor semantic content, as for example by requiring participants to find a target ‘o’ amongst ‘x’ distractors.

Another relevant aspect of search paradigms is the number of targets. Most commonly, visual search tasks showing an advantage in ASD have required locating one single target amongst distractors. In contrast, everyday selective attention often requires us to navigate a complex visual world to locate many items. Is ASD search superiority apparent when not one but multiple targets have to be found? Multiple target search requires additional cognitive skills such as good organization and planning. Based on the proposal that ASD traits confer “systematicity” (Baron-Cohen, 2009), one might expect better search organization and therefore even better search performance in multiple target displays. The relatively small literature investigating visual search as the ability to cancel / find multiple targets (“cancellation” henceforth) is mixed, with some finding poorer performance in ASD and others finding no differences compared to neurotypical controls (Goldstein, Johnson, & Minshew, 2001; Minshew, Goldstein, & Siegel, 1997; Pascualvaca, Fantie, Papageorgiou, & Mirsky, 1998). However, these studies used relatively simple measures of performance, such as omission and commission errors and time to completion. Pellicano and colleagues (2011)
employed more complex measures of search paths, instructing children to find a single hidden target amongst multiple search locations in a “foraging room,” and showed less optimal (longer distance to the target) and less systematic (reduced search consistency from trial to trial) search in children with ASD compared to neurotypical children. Thus, despite being potentially better at initially spotting targets, children with ASD might not take the most optimal route to scanning and sampling the environment, which would mitigate their strengths when faced with richer environments. Another hypothesis has been less investigated is that poor search organization might be actually the result of common co-occurring conditions. Clinical ADHD or ADHD traits have been described in children with ASD and in populations at-risk for ASD (Ozonoff et al., 2014; Simonoff et al., 2008). Approximately 20% of ASD children aged 7 in the UK meet the diagnosis of ADHD and vice versa (Russell, Rodgers, Ukoumunne, & Ford, 2014). ADHD has been linked to poorer visual search with single targets (Mullane & Klein, 2008), as well as more disorganized large-scale search (Rosetti et al., 2016).

In the current study, we investigate whether the search superiority conveyed by ASD traits holds when the nature of the target distractor distinction is varied in a multi-target search which requires planning and search organization. We asked these questions in a sample of 3-year-olds who are at familial risk for ASD due to having an older sibling with this disorder, as well as in low-risk controls. About 20% of younger siblings develop ASD themselves (Ozonoff et al., 2011) and another 20% will manifest subthreshold ASD symptoms and/or developmental delay (Messinger et al., 2013) as well as other conditions, such as increased ADHD traits (Ozonoff et al., 2014).

The broader spectrum of symptom severity in at-risk populations offers a unique opportunity to investigate the association between search skills and dimensional phenotypic measures, in accordance with recent Research Domain Criteria (RDoC, Insel et al., 2010). A
recent shift away from categorical diagnostic boundaries and towards a continuous characterization of childhood psychopathology has been motivated by both clinical and genetics findings (Plomin, Haworth, & Davis, 2009). The identification of genetic risk factors is believed to rely on the dimensional characterization of clinical phenotypes. This framework suggests that categorical disorder groups, including ASD and ADHD, are in fact each the extremes on particular continua of behavior seen across the entire population, as opposed to separate groups of individuals discriminated by clear diagnostic boundaries. Researchers are therefore encouraged to move beyond group comparisons to investigate relationships with symptoms as continuous variables, as we do in the current study.

We tested 3-year-olds at both high and low familial risk for ASD in three search conditions: easy exemplar search (look for a specific example of a cat amongst artefacts), difficult exemplar search (look for a specific example of a dog amongst chairs/tables, chosen to be perceptually similar to dogs in overall shape and color), and categorical search (look for several examples of animals amongst artefacts). We hypothesized that, compared to exemplar search, high ASD symptoms and/or an ASD diagnosis would relate to poorer performance in categorical search, where categorical knowledge has to be called upon to sift through various exemplars. ASD symptoms could potentially enhance performance in difficult exemplar search, where fine grained discriminations in shape and colour need to be made, consistent with the previous literature in fully diagnosed older ASD cases. We also predicted that co-occurring ADHD symptoms would relate to poor performance and disorganized search in this population.

Methods

Recruitment
Participants took part in a prospective longitudinal study of infants at high- and low-familial risk for autism (hereafter, HR and LR) recruited as part of the [XXX] Study. Families enrol when their babies are younger than 10 months of age, and they are invited to attend multiple research visits until their children reach 3 years of age. At the time of enrolment, none of the infants had been diagnosed with any medical or developmental condition. 116 HR participants and 27 LR participants took part in the longitudinal study. The data presented in this paper was collected during the last visit, at 3 years of age. 106 HR (60 boys, 46 girls) and 25 LR (14 boys, 11 girls) participants contributed data to this study. However, several children were not included in analyses due to missing data (see below), resulting in only 98 HR and 23 LR children. Participant characteristics for those included in analyses are below.

HR infants had at least one older sibling (hereafter, proband) with a community clinical diagnosis of ASD (96 probands were male, 10 were female). An expert clinician (TC) confirmed proband diagnosis based on information using the Development and Well Being Assessment (DAWBA; Goodman, Ford, Richards, Gatward, & Meltzer, 2000) and the parent-report Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003). Most probands met criteria for ASD on both the DAWBA and SCQ (n = 72). While a small number scored below threshold on the SCQ (n = 8), no exclusions were made, due to meeting threshold on the DAWBA and expert opinion. For 8 probands, data were only available for the DAWBA and for 16 probands data were only available for the SCQ. For 3 probands, neither measure was available aside from parent-confirmed local clinical ASD diagnosis at intake. Parent-reported family medical histories were examined for significant medical conditions in the proband or extended family members, with no exclusions made on this basis.
Infants in the LR control group were recruited from a volunteer database. Inclusion criteria included full-term birth, normal birth weight, and lack of any ASD within first-degree family members (as confirmed through parent interview regarding family medical history). All LR participants had at least one older sibling. Screening for possible ASD in these older siblings was undertaken using the SCQ, with no child scoring above instrument cut-off for ASD (1 score missing). Although a study of emerging ASD and ADHD symptoms would have recruited a large group of LR infants, our longitudinal study aimed more specifically to characterise symptoms categorically. For this reason, we oversampled HR cases, restricting the LR sample to provide a group-based comparison for the prospected 20% of infants in the HR group whom we hypothesised, based on the prior literature, to achieve a full ASD diagnosis at 3 years of age. Although this precludes us from confidently assessing whether similar associations with ASD/ADHD symptoms are found in a low-risk and a high-risk sample, this sample allows us to test for association with the broader phenotype, which is expected to span a continuum of symptoms, from typically developing to clinically diagnosed cases, in the general population.

Twenty-nine of the HR children underwent an earlier intervention (Green et al., 2015). To assure that this intervention did not interfere with the results of the current study, recruitment (being enrolled in the intervention, irrespective of whether the children were in treatment or control group) or the intervention itself (i.e. being in the treated arm of the RCT intervention or in a non-RCT intervention) were entered as a between subjects factor. There were no significant effects related to these factors and therefore these results are not mentioned further.

**Stimuli**

Target and distractor items were chosen from Snodgrass and Vanderwart-like images (Rossion & Pourtois, 2004). All stimuli drawn from this image database were normed for
visual complexity characteristics, name agreement in children as young as six years of age and were chosen for the (early) age of acquisition of their name (Cycowicz et al., 1997). For *categorical search*, targets were animals (bears, camels, cats, cows and dogs; one exemplar of each) and distractors were inanimate objects (baskets, barrels, belts, bread and bells; one exemplar of each). For the *easy exemplar search*, targets were cats (one exemplar) and distractors were inanimate objects (baskets, barrels, belts, bread and bells; one exemplar of each). For the *difficult exemplar search*, targets were dogs (one exemplar) and distractors were various chairs and tables that were perceptually similar to the dog exemplar (Figure 1). Stimuli were presented on an Elo AccuTouch 17-in touchscreen monitor with 1280 by 1024 resolution using E-prime.
Fig. 1. Top left: Example search for categorical search. Top right: Example search for the easy exemplar search. Bottom: Example search for the difficult exemplar search. Boxes surrounding targets and distracters were 1.25 x 0.94 inches on a 14.94 x 11.94 inch screen.

Procedure

These tasks were adapted from those previously used with children aged 3-6-years old (Steele, Karmiloff-Smith, Cornish, & Scerif, 2012). Children could engage in up to six runs, two of each per condition. For each run, participants were presented with a search display on the touch screen and required to touch multiple targets (up to 18) in succession. Each display contained 20 target and 70 distractor items in pseudo-random position. Children were asked to search for and touch the a) cats in the easy exemplar search, b) animals in the categorical search, and c) dogs in the difficult exemplar search. The easy and difficult exemplar searches were always run after the categorical search, so as not to bias children to look for specific items (cats/dogs) which would diminish the extent to which the categorical condition tested their category knowledge. The order of condition presentation was the same for all children: 1) conceptual, 2) easy exemplar, and 3) difficult exemplar. Instructions: “Can you find all the [animals]? When you touch them, you'll find a star.” When children successfully touched a target, a star appeared on the screen and remained there for the duration of the run. When children touched a distractor there was no feedback. There was no time limit for a run, instead the run ended when children touched a total of 18 targets or 40 responses were made overall. Children were given neutral reinforcement to keep them engaged—“keep going!”

See Table 1 for information of how many children completed at least one run in each condition.

Table 1

| Number of participants who completed two runs (or one run only, in parentheses) of each search type by categorical group for sample included in analyses |
|----------------------|----------------|----------------|----------------|----------------|----------------|
| LR(23) | HR(98) | HR-typical(56) | HR-atypical(28) | HR-ASD(14) |
Search organization and autism symptoms

<table>
<thead>
<tr>
<th>Categorical</th>
<th>22(1)</th>
<th>94(4)</th>
<th>55(1)</th>
<th>26(2)</th>
<th>13(1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy exemplar</td>
<td>20(3)</td>
<td>84(4)</td>
<td>53(1)</td>
<td>2(1)</td>
<td>0(2)</td>
</tr>
<tr>
<td>Diff exemplar</td>
<td>19(1)</td>
<td>77(7)</td>
<td>47(4)</td>
<td>21(1)</td>
<td>9(2)</td>
</tr>
</tbody>
</table>

Note: LR = low risk, HR = high risk. Total number of participants in parentheses in table heading. See below for descriptions of categorical groups.

Outcome characterisation

Standard measures of cognitive development (Mullen Scales for Early Learning (MSEL); Mullen, 1995) and adaptive development (Vineland Adaptive Behavior Scales; Sparrow, Balla, & Cicchetti, 2005) were collected. The MSEL is a standardised direct developmental assessment that yields a standardized score (mean = 100, SD = 15) of overall intellectual ability (Early Learning Composite), and subscale T-scores (mean = 50, SD = 10) for receptive language (RL) and expressive language (EL), as well as non-verbal fine motor (FM) and visual reasoning (VR) abilities. The Vineland is a standardised parent-reported interview of everyday adaptive functioning that measures social, communication, daily living and motor skills.

The Autism Diagnostic Observation Schedule – Second Edition (ADOS-2; Lord et al., 2012), a standardised interaction observation assessment, was used to assess current symptoms of ASD (114 children were administered Module 2 and 17 children Module 1). Calibrated Severity Scores for Social Affect (SA), Restricted and Repetitive Behaviours (RRB) and Overall Total were computed (Gotham, Pickles, & Lord, 2009; Hus, Gotham, & Lord, 2014), which provide standardised autism severity measures that account for differences in module administered, age and verbal ability. The Autism Diagnostic Interview – Revised (ADI-R; Le Couteur, Lord, & Rutter, 2003), a structured parent interview, was completed with parents of HR children. Standard algorithm scores were computed for Reciprocal Social Interaction (Social), Communication, and Restricted, Repetitive and Stereotyped Behaviours and Interests (SBRI). These assessments were conducted without
blindness to risk-group status by or under the close supervision of clinical researchers (i.e., psychologists, speech therapists) with demonstrated research-level reliability.

The Child Behavior Checklist (CBCL; Achenbach & Edelbrock, 1991) was used to assess severity of ADHD symptoms (ADHD t-scores). See Supplementary Online Materials (“SOM”) for relationships between these measures (CBCL, MSEL, ADOS).

As children in this study were 3-years-old, it was possible for a clinical ASD diagnosis to be attained. Experienced clinical researchers (TC, GP, CC) reviewed information on ASD symptomatology (ADOS-2, ADI-R, SCQ), adaptive functioning (Vineland-II), and development (Mullen) for each HR and LR child to ascertain ASD diagnostic outcome according to DSM-5 (American Psychiatric Association, 2013). From the 106 HR participants included in this paper 15 (13 boys, 2 girls) met criteria for ASD (hereafter, HR-ASD). A further 30 participants (19 boys, 11 girls) did not meet ASD criteria, but were not considered typically-developing, due either to a) scoring above ADI-R cut-off for ASD (Risi et al., 2006) (n=1), b) scoring above ADOS-2 cut-off for ASD (n=12), c) scoring greater than 1.5 SD below the population mean on the Mullen ELC (< 77.5) or on the Mullen EL or RL subscales (< 35) (n=9), or meeting both of points a or b and c above (n=8). These therefore comprised a HR subgroup presenting other atypicalities (hereafter, HR-Atypical). There is no agreed definition for a HR-Atypical group, in the field, with research teams using different clinical tools or thresholds (see Charman et al., 2017, for a discussion). We choose here to use the same criteria as we have used in previous publications from out group (e.g. Cheung et al., 2017; de Klerk et al., 2014). The remaining 61 participants (28 boys, 33 girls) were typically-developing (hereafter, HR-Typical). None of the 25 LR children met DSM-5 criteria for ASD and none had a community clinical diagnosis of ASD or any other developmental disorder. No further sub-classification of the LR group was carried out.
Search measures

To investigate search performance, two sets of measures were analyzed. The first set comprised three traditional measures of search performance: accuracy (number of hits), errors (touches to distractors), and time to completion. These measures were highly skewed and therefore these analyses are included only in the SOM. In addition, there were in fact very few children with poor accuracy. Only 18% of children in conceptual search, 4% in easy exemplar search and 4% in difficult exemplar search had average accuracy poorer than 80%. There were only 6% of children in conceptual search, 3% in easy exemplar search, and 2% in difficult exemplar with average accuracy poorer than 50%, suggesting that children were overall very accurate.

Three additional measures produced by CancellationTools software were used to investigate general search performance as well as search organization without the difficulty of skew produced by traditional measures. CancellationTools is a free, open source software that aids in both collecting and analyzing cancellation data that reduces human error associated with previous pen and paper tasks (Dalmaijer, Van der Stigchel, Nijboer, Cornelissen, & Husain, 2015). Moreover, it automatically calculates some of the most sensitive measures of search in the literature. The first measure we used, Q score, combines speed and accuracy into a single measure of search efficiency, such that Q score equals the number of correctly cancelled targets squared divided by the product of the total number of targets and the total time spent on the task. A high Q score represents a combination of a high number of cancelled targets and high speed of cancellation. This measure was first described by Hills and colleagues (1998) and has since been used in several cancellation studies investigating age and task differences (Byrd, Touradji, Tang, & Manly, 2004; Huang & Wang, 2008). Although accuracy was very high in the current study (as described above and
in the SOM), time to completion demonstrated much more variability—with a range of 16 seconds to 4 minutes and 20 seconds across all three conditions. We therefore felt that combining speed and accuracy into a Q score was justified, as a more sensitive measure than accuracy in this study that could differentiate children who were accurate and fast from accurate and slow, given that accuracy was high.

The second measure, best R, is a measure of horizontal or vertical spatial organization and is defined as “the highest absolute value of the Pearson correlation between cancellation rank number and either horizontal or vertical cancellation position” (Dalmaijer et al., 2015). A high best R represents more spatially systematic search. This measure has been used to show less spatially systematic search in stroke patients (Brink, Van der Stigchel, Visser-Meily, & Nijboer, 2015; Broeren, Samuelsson, Stibrant-Sunnerhagen, Blomstrand, & Rydmark, 2007; Mark, Woods, Ball, Roth, & Mennemeier, 2004). Best R has also been used to demonstrate how search becomes more spatially systematic over neurotypical development (Woods et al., 2013). In addition, Woods and colleagues (2013) have shown best R to relate to accuracy in single target search across development (2-17 years) and argue that increased ability to organize search helps sifting through both targets and distractors in traditional visual search tasks.

The third measure, intersections rate, quantifies the number of times the search path crosses over itself, divided by the amount of cancellations that are not immediate revisits (Dalmaijer et al., 2015). A high intersections rate reflects disorganized exploration (Brink et al., 2015; Rabuffetti et al., 2012; Woods et al., 2013).¹

¹ Important to note, there are inconsistencies in the literature in how these measures are described. While some describe both best R and intersections rate as measures of “search organization” (Woods et al., 2013), others differentiate them, for example describing best R
Statistical approach

Two statistical approaches were used. First, in accordance with the research domain criteria (RDoC) approach and a shift away from categorical diagnosis towards continuous / dimensional characterization of psychopathology (Plomin et al., 2009), we analyzed both ASD and ADHD symptoms as continuous predictors of search. Second, we investigated ASD diagnostic groups (and continuous ADHD symptoms, as ADHD is not typically diagnosed until later in childhood) as predictors of search.

ASD and ADHD symptoms as continuous predictors of search

To investigate possible relationships with ASD and ADHD symptom severity, Mixed effects models were specified using the lme4 package in R (Bates, Mächler, Bolker, & Walker, 2015). Importantly, this procedure allowed for including children with missing data in one or more conditions. For each dependent measure (Q score, best R, and intersections rate), a model was specified with a fixed effect of condition (easy exemplar, difficult exemplar, conceptual), MSEL as well as each of the three symptom severity measures (ADOS-SA, ADOS-RRB, CBCL-ADHD) as covariates, a random slope of condition, and a random effect of participant. For these models, p values were determined using the Kenward-Roger approximation for degrees of freedom (Kenward & Roger, 1997) as implemented by the afex package in R (Singmann, Bolker, & Westfall, 2015). All covariates were centered for these analyses. Although the MSEL and ADOS was completed for all children, the CBCL was not completed for 10 children. These analyses were therefore restricted to the children for which the CBCL was completed: 23 LR and 98 HR children (see Table 2 for demographics for this limited sample). Although the dependent measures were not skewed, as “search consistency” and intersections rate as “organization” (Brink et al., 2015). For clarity we use the definitions described in the text.
the covariates were slightly skewed, therefore non-parametric statistics were used when follow-up analyses included the covariates, to provide a conservative check that effects were robust to violations of the assumptions of parametric statistics. Significance level remained unchanged when removing the 14 children in the sample that received an ASD diagnosis at age 3 (see SOM).

Table 2
Participant characteristics, sample limited to those who contributed data to the analyses

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (months)</th>
<th>Gender (M:F)</th>
<th>MSEL ELC</th>
<th>ADOS-SA</th>
<th>ADOS-RRB</th>
<th>CBCL-ADHD</th>
<th>ADI-Soc</th>
<th>ADI-Com</th>
<th>ADI-SBRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (n=98)</td>
<td>38.84 (1.57)</td>
<td>55:43</td>
<td>103.94*</td>
<td>3.45</td>
<td>1.31**</td>
<td>55.45***</td>
<td>3.28***</td>
<td>3.65***</td>
<td>1.46***</td>
</tr>
<tr>
<td>LR (n=23)</td>
<td>38.52 (2.43)</td>
<td>14:9</td>
<td>118.61</td>
<td>2.83</td>
<td>0.70</td>
<td>51.04</td>
<td>0.91</td>
<td>0.48</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Note. Figures in parentheses are SDs. Mullen Scales for Early Learning, Early Learning Composite (MSEL ELC), Autism Diagnostic Observation Schedule, Social Affect (ADOS-SA), Autism Diagnostic Observation Schedule, Restricted and Repetitive Behaviors (ADOS-RRB), Child Behavior Checklist, ADHD t-scores (CBCL-ADHD), Autism Diagnostic Interview, Social (ADI-Soc), and Autism Diagnostic Interview, Restricted, Repetitive and Stereotyped Behaviours and Interests (SBRI) (see below for measure characterization). Significant differences between the HR and LR groups indicated by *p < 0.05, **p < 0.01, ***p < 0.001.

ASD diagnostic outcome as a predictor of search

To investigate possible relationships with ASD diagnostic outcome, mixed effects models were specified with condition as a fixed effect (easy exemplar, difficult exemplar, categorical) MSEL as well as CBCL-ADHD as covariates, a random slope of condition, and a random effect of participant for all three dependent measures (Q score, best R, and intersections rate). All covariates were centered for these analyses. As mentioned above, not every child had a complete CBCL. Of those who did, there were 14 in the ASD group, 28 were HR-atypical, and 56 were HR-typical (23 in the LR group), and these are the children contributing to the analyses below.

Results

ASD and ADHD symptoms as predictors of search
For **Q score**, our index of overall search efficiency, there was a significant effect of condition, $F(2, 99.67) = 95.64, p < 0.001$. This effect was driven by Bonferroni-corrected significant differences among conditions (all $p < 0.001$), with easy exemplar search yielding the highest Q score, perceptual search with the next highest and categorical search with the lowest (see table 3 for descriptives). There was a condition by ADOS-SA interaction, $F(2, 108.37) = 3.69, p = 0.03$. Following up this interaction with non-parametric Spearman’s Rho correlations for each condition revealed a significant negative correlation between ADOS-SA and Q score in the categorical search condition, $r(120) = -0.20, p = 0.025$, with higher ASD symptoms related to low Q score (less efficient search), but no significant correlations in the other two conditions ($p > 0.250$). There was also a significant effect of MSEL, $F(1, 113.80) = 30.04, p < 0.001$, with higher developmental ability related to higher Q scores (greater speed and accuracy). All MSEL subscales scales, when entered in the model separately, related to performance (motor, $F(1, 112.30) = 21.10, p < 0.00$; visual reception, $F(1, 114.87) = 20.49, p < 0.001$, receptive language, $F(1, 112.54) = 15.18, p < 0.001$; expressive language, $F(1, 114.03) = 24.05, p < 0.001$), suggesting that it was not poor motor skills or poor understanding of instructions that particularly affected performance. Including these scales in the model did not change the significance level of the other factors or interactions.

Table 3

<table>
<thead>
<tr>
<th>Measure</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Categorical</td>
</tr>
<tr>
<td>Q score</td>
<td>0.27(0.15)</td>
</tr>
<tr>
<td>Best R</td>
<td>0.48(0.15)</td>
</tr>
<tr>
<td>Intersections rate</td>
<td>0.28(0.22)</td>
</tr>
</tbody>
</table>

Figures in parentheses are SDs. Sample limited to those children who contributed data to the analyses.
For **best R**, our index of spatial systematicity, there was a significant effect of condition, $F(2, 102.57) = 6.97$, $p = 0.001$. This effect was driven by Bonferroni-corrected significantly lower best R for categorical search compared to easy exemplar search ($p < 0.001$), and difficult exemplar search ($p = 0.024$), but no significant difference between the latter two ($p > 0.250$) (see table 2). There was also a significant effect of CBCL-ADHD, $F(1, 112.68) = 7.42$, $p = 0.007$, with higher ADHD symptom severity related to lower best R (more spatially unsystematic search). Moreover, including the expressive language and receptive language scales did not affect the results and were not significant covariates when used instead of the MSEL Q score and best R did not relate to each other (see SOM).

For **intersections rate**, our index of spatial organization, there was a significant effect of condition, $F(2, 104.48) = 15.14$, $p < 0.001$. This was driven by Bonferroni-corrected significantly higher intersections rate for categorical search compared to difficult exemplar search ($p < 0.001$) and easy exemplar search ($p < 0.001$), but no difference between the latter two ($p > 0.250$) (see table 2). There were also significant effects of three of the covariates: ADOS-SA, $F(1, 123.35) = 5.21$, $p = 0.02$, ADOS-RRB, $F(1, 113.29) = 5.33$, $p = 0.02$, CBCL-ADHD, $F(1, 114.97) = 11.58$, $p < 0.001$, with higher scores on the ADOS-SA, ADOS-RRB and CBCL-ADHD related to higher intersections rates (i.e., more disorganized search). There was also a non-significant trend toward an effect of MSEL, $F(1, 115.02) = 3.40$, $p = 0.07$, with lower scores on the MSEL related to higher intersections rates (i.e., more disorganized search). Again, including the fine motor, visual reception expressive language, and receptive language sub-scales separately or removing the Mullen altogether, did not affect the main effects of clinical traits. The main effect of ADOS-RRB was further qualified by an ADOS-RRB by condition interaction, $F(2, 106.62) = 4.44$, $p = 0.01$. To follow up this interaction, non-parametric Spearman’s Rho correlations were run for each condition, revealing a significant positive relationship between ADOS-RRB and intersections rate in the
perceptual condition only, $r(104) = 0.21, p = 0.036$, suggesting that the more severe restricted interests and repetitive behaviors were, the least organized search was, but no significant correlations in the other two conditions ($p > 0.250$). Intersection rate negatively correlated with Q score, with more disorganized search related with poorer search performance (see SOM for details).

In light of the main effects of CBCL-ADHD and ADOS-SA without further interactions with condition (i.e. only ADOS-RRB interacted with condition), another model was run in order to determine if the main effects were further qualified by an interaction between the symptoms. The main effects remained, but the interaction term was not significant ($p > 0.250$), which is compatible with independent contribution from ASD and ADHD symptoms.

**ASD diagnostic outcome as a predictor of search**

In addition to using a continuous measure of ASD symptoms as a predictor, we investigated ASD diagnostic outcome as a fixed effect. However, these analyses are prefaced by caution, given limited statistical power and uneven Ns (only 14 in the HR-ASD group but 56 in the HR-Typical group). In addition, as seen in Table 2, there were significant differences in covariates between HR and LR groups, which makes including a between-subjects effect inappropriate due to the statistical assumptions of covariate analyses, further adding to our caution (Miller & Chapman, 2001). Here we report inferential statistics for readers interested in pursuing replication with a larger sample, but we will focus on the continuous symptom analyses for our discussion. See Supplementary Tables for descriptives.

For **Q Score**, there was an effect of condition, $F(2, 101.01) = 63.19, p < 0.001$, and MSEL, $F(1, 113.97) = 20.57, p < 0.001$, with higher developmental ability related to higher Q scores (greater speed and accuracy).
For **Best R**, there was only an effect of condition, $F(2, 103.79) = 6.17$, $p = 0.003$ and CBCL-ADHD, $F(1, 111.89) = 7.17$, $p = 0.009$, with higher ADHD symptom severity related to lower best R (more spatially unsystematic search).

For **intersections rate**, there was an effect of condition, $F(2, 105.64) = 13.81$, $p < 0.001$, and CBCL-ADHD, $F(1, 114.32) = 4.98$, $p = 0.03$, with higher scores on CBCL-ADHD related to higher intersections rates (i.e., more disorganized search).

**Discussion**

The current study utilized a multi-target visual search cancellation task with naturalistic objects as targets and distractors in a sample of 3-year-old children with an older sibling with ASD - a population that presents high ASD and ADHD symptoms. The study sought to answer the question: do ASD symptoms and/or an ASD diagnosis as well as ADHD symptoms relate to search efficiency, systematicity and organization in varying search conditions? More specifically, does poor performance in categorical search, where targets represent a category (animals), and enhanced performance in perceptual search, where targets are perceptually similar to distractors, relate to high ASD symptom severity and/or an ASD diagnosis, consistent with previous literature? In addition, how do co-occurring ADHD symptoms relate to search performance?

Before discussing ASD and ADHD symptoms, it is important to note that for all three measures of search performance and organization, categorical search in general proved more difficult than exemplar search as we hypothesized. This is consistent with the recent literature investigating categorical search with single targets and realistic target and distractor objects (Maxfield & Zelinsky, 2012; Schmidt & Zelinsky, 2009) and extends this finding to multi-target search cancellation as well as, for the first time, to a very young population of children.
Although this may be due to difficulty with category knowledge, particularly given the young age of participants, previous literature has shown similar difficulty in adults (Maxfield & Zelinsky, 2012; Schmidt & Zelinsky, 2009). It is possible that poorer performance in categorical search is due to the lack of perceptual specificity that helps to guide visual search to realistic, complex objects, or the tendency to combine instances of a category into a prototype that has little overlap with specific search target exemplars, as has been suggested previously (Hout & Goldinger, 2015; Yang & Zelinsky, 2009; Zhang et al., 2006).

In addition, for Q score, our measure of efficient search, searching for dogs amongst perceptually similar furniture items proved more difficult than searching for cats, again as we hypothesized. This increased difficulty is consistent with the vast single target search literature using simple targets and distractors (Duncan & Humphreys, 1989; Treisman, 1991) as well as single target search using more realistic objects (Alexander & Zelinsky, 2011), and again extends this finding to multi-target search cancellation as well as to a very young population.

**Association of clinical measures with search performance**

**Search efficiency (Q score).** Both ASD and ADHD symptoms related to search efficiency, but not always in the direction hypothesized given the prior literature. First, our measure of ASD symptoms, the ADOS-SA, related to search efficiency in the categorical search condition specifically, with lower speed/accuracy (Q score), i.e., lower efficiency, associated with high ADOS-SA scores. This confirmed our hypothesis based on the literature on diagnosed cases of ASD suggesting difficulties with categorical knowledge (Naigles et al., 2013). One might expect that difficulty with representing categories might lead children at risk to adopt a strategy in which they search for each basic level of the category sequentially, ASD symptom severity did not relate to more frequent use of this strategy (SOM). Although the specific mechanism behind this impairment could not be determined by the current study,
some researchers argue that, in ASD, impaired categorical knowledge depends on a relative enhanced ability to determine how things are different and a difficulty determining how things are the same (Soulières, Mottron, Giguère, & Larochelle, 2011; Soulières, Mottron, Saumier, & Larochelle, 2006).

However, ASD symptoms did not relate to better search efficiency in the difficult exemplar search condition, where target and distractor are perceptually similar, contrary to our original hypothesis derived from research with children with diagnosed ASD. A significant literature demonstrates that individuals with ASD (e.g. Plaisted et al., 1998) as well as those with high autism-like traits (Brock, Xu, & Brooks, 2011) perform better in difficult visual search conditions when targets and distractors are perceptually similar. Researchers have argued this is due to an enhanced perceptual ability to discriminate features (Joseph, Keehn, Connolly, Wolfe, & Horowitz, 2009; Kaldy et al., 2016; O'Riordan & Plaisted, 2001; Swettenham, Lavie, & Remington, 2012). However, we did not replicate these findings when using multi-target cancellation with more realistic target and distractor objects. Indeed, high ADOS-RRB was associated with greater disorganization (intersections rate) in the difficult exemplar condition in particular. Of note, this association differentiated ADOS-RRB from the ADOS-SA dimension in our sample, as has been suggested can be the case in the spectrum as a whole (Happe’, Ronald, & Plomin, 2006). Newer evidence for an association between single target search and pupil dilation led to the proposal that what differentiates participants with ASD is their ability to search more items at a time (Blaser et al., 2014). While this proved to be an advantage when searching for one item, in Blaser et al., this may not help in our study where many items can be spotted at each fixation. Having to keep in memory these items or to decide which one to go for may trade off search advantages, in our study. Alternatively, it is possible that perceptual superiority is specific to particular features, such as line orientation (Dickinson, Jones, & Milne, 2014).
**Systematicity (best R)**

Second, ADHD symptoms, but not ADOS-SA scores related to search systematicity (best R), with poorer systematicity associated with higher ADHD symptoms across all three conditions. Although the lack of a relationship with ASD symptoms may appear surprising given Pellicano and colleagues’ (2011) finding of poorer systematicity by children with ASD in their foraging task, this may be due to task differences. Pellicano and colleagues’ (2011) measured systematicity as consistent search *across* trials, e.g. starting search on the left side, which they argue relates to inferring and capitalizing on rules, whereas here we measured systematicity in spatial search pattern within runs, e.g. searching all targets in a line. We believe this to be more indicative of planning than rule use, as there were no similar rules to be inferred in the current task. In addition, the relationship with ADHD symptoms confirms our initial hypotheses based on the previous literature of both large and small scale search (Mullane & Klein, 2008; Rosetti et al., 2016).

**Search organization (intersections rate)**

Third, for search organization (intersections rate), high ADOS-SA and ADHD scores both contributed to more disorganized search, across search conditions. Thus, in this sample, the relationship between ASD symptoms and disorganized search was not explained by ADHD symptoms alone, but rather levels of both symptoms contributed independently to poor search organization. This finding is relevant to the literature investigating comorbid ASD and ADHD symptoms that has developed over the past decade. Some hypothesize that, even within a single domain such as attention, ASD and ADHD are associated with different types of impairments such as comorbid ASD and ADHD will demonstrate both sets of impairments (Sinzig, Bruning, Morsch, & Lehmkuhl, 2008; e.g. Tye et al., 2014), or sometimes, when ASD and ADHD associate with opposite attention patterns, to a cancelling out of effects (Gliga, Smith, Likely, Charman, & Johnson, 2015b; van der Meer et al., 2014).
Yet another perspective suggests that attentional impairment only occurs with the presence of ADHD, either in “pure” cases or comorbid ASD and ADHD, which would mean that ADHD is the source of atypicalities of attention associated with ASD. Our results with search organization (intersections rate) suggest a mixed picture, with ASD and ADHD symptoms contributing independently to exacerbate the same attentional impairment (Yerys et al., 2009). However, we have tested a limited number of models of how ASD and ADHD symptoms themselves may interact (by analyzing models with and without the ASD-by-ADHD interaction term), which does not address fully the complexity of partially overlapping psychopathological dimensions.

Interestingly, although both ASD and ADHD symptoms were related to poorer search organization in general across conditions, ADHD symptoms did not relate to poor search efficiency and ASD symptoms only related to poor search efficiency in categorical search. This was despite the fact that more organized search (lower intersections rate) was generally associated with better search efficiency (higher Q score) (see SOM). The lack of a relationship between search organization and search efficiency in the context of ASD and ADHD symptoms is interesting as it suggests that rather than indexing an “impairment” (poorer performance) these measures point to the existence of compensatory strategies that allow certain individuals to succeed in the search task despite adopting atypical foraging strategies. In other words, despite poorer search organization in children with high ASD and/or ADHD symptoms, these children were just as efficient (with regard to high speed/accuracy) as those with low ASD and/or ADHD symptoms.

**Limitations and Future Directions**

There are several limitations of the study that should be mentioned. One is that the diagnosis of the proband was not confirmed with a gold standard measure such as the ADOS,
but only by parent report. However, in common with many other high-risk sibling studies, the information from these assessments was reviewed by an experienced clinician (TC) and in combination with local clinical diagnosis by community services we are confident that the families did have an older child with an ASD diagnosis. Another limitation is that although the full sample was 131 children participating in the study, due to missing data the sample used for analysis was only 121 children. Although this represents excellent retention and data completion for an intensive study that spanned the children’s first 3 years of life, replications of our findings on larger samples, potentially seen at only one time point, are welcome. In addition, the current LR group was not adequately sized to ask questions about search indices in the general population, as the low-risk sample was recruited in infancy purely as a comparison group to our prospected final sample of HR-ASD 36-month-olds. Future studies in typically developing 3-year-olds could investigate in depth how distinct indices of search performance and organisation relate to typically developing children’s broader profile of cognitive and mental health.

Perhaps the most important limitation is the sample size with respect to ASD diagnostic group. Infant recruitment for this study was designed for following risk longitudinally, we did not simply recruit children at 3-years. the sample size of HR infants was determined based on previous infant at risk studies suggesting 20% of HR infants later meet diagnostic ASD criteria (Ozonoff et al., 2011). However, the number of infants at risk that eventually met diagnostic ASD criteria in the current study (the HR-ASD group) was relatively small (17/116 recruited, 15%). It is therefore difficult to draw strong conclusions from the null findings in terms of clinical outcomes. For categorical analysis a different approach, investigating larger samples of children with community diagnosis of ASD, would be more appropriate.
Finally, a recent eye-tracking study on visual processing in children with ASD suggests that investigating behavioral performance on its own may not be sensitive enough to capture atypical processing characteristic of ASD (Nayar, Voyles, Kiorpes, & Di Martino, 2017). Objective indices that more directly take into account underlying physiology may provide a more complete picture of search strategies related to ASD.

**Conclusion**

In conclusion, our study suggests that the search superiority thus far associated with ASD symptoms may only be evident under restricted experimental conditions, including single target search with targets/distractors distinguished by few visual features. In our multi-target cancellation task with more complex targets/distractors, ASD symptoms were associated with more disorganized search across conditions, and poorer search performance for categorical search in particular. In addition, ADHD symptoms contributed to search disorganization, which further reinforces the research domain criteria call to investigate multi-dimensional contributions to cognitive profiles.

**Acknowledgements**

This research was supported by: a Rhodes Scholarship and Clarendon Scholarship to B. Doherty, an Understanding Human Cognition James S. McDonnell Foundation Scholar Award to G. Scerif, a Medical Research Council (MRC) Program Grant G0701484 to M. H. Johnson, and the BASIS funding consortium led by Autistica (www.basisnetwork.org). This work was also supported by EU-AIMS (European Autism Interventions), which receives support from the Innovative Medicines Initiative Joint Undertaking under grant agreement no. 115300, the resources of which are composed of financial contributions from the European Union's Seventh Framework Programme (grant FP7/2007-2013), from the
European Federation of Pharmaceutical Industries and Associations companies’ in-kind contributions, and from Autism Speaks. We would also like to acknowledge collaboration with A. Steele, K. Cornish and A. Karmiloff-Smith that generated the initial version of the search task used here, as well as A. Karmiloff-Smith for her continuing inspiration in developmental science.

References
Search organization and autism symptoms


Search organization and autism symptoms 31


