

Brief Report: Autism-like Traits are Associated With Enhanced Ability to Disembed Visual Forms

Antoinette Sabatino DiCriscio¹ · Vanessa Troiani¹

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Abstract Atypical visual perceptual skills are thought to underlie unusual visual attention in autism spectrum disorders. We assessed whether individual differences in visual processing skills scaled with quantitative traits associated with the broader autism phenotype (BAP). Visual perception was assessed using the Figure-ground subtest of the Test of visual perceptual skills-3rd Edition (TVPS). In a large adult cohort ($n=209$), TVPS-Figure Ground scores were positively correlated with autistic-like social features as assessed by the Broader autism phenotype questionnaire. This relationship was gender-specific, with males showing a correspondence between visual perceptual skills and autistic-like traits. This work supports the link between atypical visual perception and autism and highlights the importance in characterizing meaningful individual differences in clinically relevant behavioral phenotypes.

Keywords Broader autism phenotype · Visual attention · Perception · Individual differences · Gender differences · Figure-ground discrimination

Introduction

Individuals with autism spectrum disorder (ASD) are frequently described as “missing the forest for the trees”. In some experimental settings, this focus on details can emerge as a relative strength, particularly in visual tasks

that require the prioritization of detailed (local) information from a contextual (global) whole. Empirical research indicates that individuals with ASD can demonstrate superior performance on perceptual tasks such as the block design portion of intelligence tests, where smaller features must be isolated within a larger whole (Stewart et al. 2009). This phenomenon has been given several names, including a “perceptual advantage” or “islet of ability” (Dakin and Frith 2005; Happe 1999; Simmons et al. 2009) and has been consistently observed in visuospatial tasks requiring focused attention and the prioritization of local (part-based) relative to global (whole) information (i.e. embedded figures, visual search tasks) (for review see Dakin and Frith 2005; Mottron et al. 2006; Plaisted et al. 1998; Simmons et al. 2009; Jolliffe and Baron-Cohen 1997; O’Riordan 2004; O’Riordan et al. 2001; Kaldy et al. 2011, 2013).

This prioritization of local processing in ASD has also been explained as an atypical bias to process local information (local precedence) in ASD (Scherf et al. 2008), which stands in contrast to a global precedence effect in typical controls (Navon 1977, 1981), with most individuals perceiving a perceptual whole prior to local parts. However, there appears to be natural variability in global relative to local processing across the general population (Dale and Arnell 2013; McKone et al. 2010; Scherf et al. 2009). Thus, meaningful individual differences in global versus local precedence may reflect a distribution of visual processing strategies that reveal an important cognitive trait.

Autistic-like traits (ALTs) that are below the clinical threshold for diagnosis and commonly found in at least one parent of children with ASD were first described as the broader autism phenotype (BAP). More recently, this term has been adopted to describe subclinical traits in the broader population that are continuously distributed (Hoekstra RA, Bartels Verweij CH, & Boomsma DI,

✉ Antoinette Sabatino DiCriscio
asdcriscio@geisinger.edu; sabatino.antoINETTE@gmail.com

¹ Geisinger Health System, Geisinger Autism and Developmental Medicine Institute (ADMI), Lewisburg, PA 17837, USA

2007). Quantitative measures of ALTs across the BAP have been developed (Hurley et al. 2007) and a number of studies have documented a variable range of social functioning and cognitive traits consistent with an ASD diagnosis among typically developing adults (Martino, Adriana et al. 2009; Ingersoll 2010; Jobe and White 2007). ALTs in typical young adults correlate with visual-perceptual abilities (Almeida et al. 2010b; Bayliss and Kritikos 2011), with those scoring higher on ASD rating scales outperforming peers in areas of visual discrimination and spatial processing. Findings such as these, from non-clinical samples, emphasize the importance of characterizing the BAP and using objective, quantitative measures of ALTs to describe the natural variability of clinically relevant phenotypes across the general population.

Recent studies have highlighted inconsistent findings of heightened visual performance across the BAP. There are several possible explanations regarding discrepant findings in previous research including methodological approaches, sample (size and characterization of groups), as well as choice of behavioral measures. Much of the current literature employs the EFT (Witkin 1971) in conjunction with the autism spectrum quotient (AQ; Baron-Cohen et al. 2001), a self-report measure of autism traits, in the general population (Almeida et al. 2010a, b; Grinter; Maybery et al. 2009; Grinter et al. 2009; Russell-Smith et al. 2010). Frequently, individuals are grouped based upon low-AQ relative to high-AQ scores (i.e. highest and lowest 15%) (Gregory and Plaisted-Grant 2013). A meta-analysis of these studies (Cribb et al. 2016) reported that higher performance in the EFT is related to the ALTs when comparing these dichotomous subclinical groups (high versus low autism traits); however, those studies that considered AQ scores as continuous variables failed to identify enhanced visual perception in those with higher autism traits. Using a Monte-Carlo simulation, Cribb et al. (2016) demonstrated that larger samples are necessary for the continuous measurement of autism traits and quantifying the relationship with visual perceptual features. In the embedded figures test (EFT), an individual is required to identify a simple shape within a more complex design. On each of the 25 test items, the simple shape to be identified comes from a finite set of four shapes. In the children's version of the EFT, individuals are asked to find the same shape repeatedly (a triangle or "tent" then a "house") across the two blocks of the test (i.e. participants complete the 11 "tent" test items before moving on to the 14 "house" test items).

Although no previous studies have investigated the relationship between individual differences in visually disembedding information (as in the EFT and other assessments of visual perceptual skills) and ALTs, previous work has linked atypical visual processing and overall autism traits (Robertson et al. 2014) as measured by the

autism diagnostic observation schedule (ADOS) (Lord et al. 2000). This suggests that visual perceptual anomalies may be linked with autism traits or symptom severity more generally. However, other work has shown that atypical visual attention is linked specifically with social symptoms (Antezana et al. 2016; Frischen et al. 2007; Klin et al. 2002). Taken together, it remains uncertain whether atypical visual attention is related to overall autism traits or more specific characteristic symptom domains.

To our knowledge, no study to date has made use of other standardized perceptual tests that require the identification of a different simple shape on each test item in order to quantify perceptual strengths across the BAP within a large sample. In the current study, we made use of the figure ground subtest of the test of visual perceptual skills-3rd edition (TVPS-3). This particular subtest is based upon similar hierarchical visual processing principles as those in the EFT. Individuals are asked to identify a simple image nested within a more complex shape. The simple and complex shapes are different for each test item; thus, individuals are not being asked to repeatedly identify the same shape (or a finite set of shapes) across test items. One notable difference between the EFT and TVPS-3 is that in the EFT the same visual target shape (or finite set of target shapes) is used for every trial; whereas, in the TVPS, the target shapes and surrounding distractors are unique across all trials. We assessed the presence of ALTs using the broader autism phenotype questionnaire (BAP-Q) (Hurley et al. 2007), a self-report measure that provides an overall average score of autism symptoms as well as scores across three subscales (Social Aloofness, Pragmatic Language, and Rigidity) directly relevant to core diagnostic categories for ASD. In comparison to other quantitative measures of ALTs such as the AQ, the BAP-Q has been noted for its reliable measurement of traits central to the autism phenotype (Cribb et al. 2016; Nishiyama et al. 2014). We predicted that TVPS-Figure Ground (TVPS-FG) scores would be directly related to BAPQ scores, with higher TVPS scores correlating with a greater number of ALTs. We also explored gender differences in visual perception and the relationship to ALTs across males and females.

Methods

Participants and General Procedure

Participants ($n = 209$; mean age = 41.68 ± 11.59 ; 105 males) included individuals 18 years of age and older within the United States, identified via Amazon Mechanical Turk (<https://www.mturk.com/mturk/>), an online data collection mechanism supported by Amazon.com. Mechanical Turk has been used to replicate

several psychology experiments online (Horton et al. 2011; Mason and Suri 2012; Paolacci et al. 2010), making it a useful resource for acquiring data in a diverse, scalable sample. Sample demographics can be found in Tables 1 and 2.

All measures were adapted for online use using Testable (<http://www.testable.org/>) and administered via Amazon Mechanical Turk, an online based “marketplace” by which individuals, researchers or businesses can post “work” or Human Intelligence Tasks (HITs). Interested “workers” (i.e. participants) are able to create a login to Mechanical Turk, view available HITs, and complete those tasks at their convenience. Once a HIT is completed, participants are compensated via Amazon Mechanical Turk thru a pre-paid account owned by the researcher. Participants were identified based upon the following selection criteria: (1) currently residing within the United States; (2) had obtained a Mechanical Turk user approval rating of >90%; and (3) completed >500 HITs, and thus considered a Masters level user. All participants completed an online consent approved by the authors’ home institution’s ethical review board prior to completing the measures described below. It was indicated to participants that task completion would take approximately 25 min. If participants were unable to complete the measures within a 2 h time frame, their HIT session was timed out and their data was excluded from the study. Also, a total of 3 simulated test items were administered throughout the online administration of the TVPS-FG to ensure that participants were engaged in the task and were not providing invalid data. These items were over simplified yet appeared similar to test items.

Table 2 Frequency table of education and ethnicity

	Frequency
Education	
Less than high school	4
Completed high school	45
Associate/Technical degree	63
Bachelor’s degree	73
Masters/Doctorate degree	24
Ethnicity	
Caucasian	171
Hispanic/Latino	8
African American	11
Native American	1
Asian/Pacific Islander	15
Other	3

All participants accurately answered at least 2 of these simulated items

Behavioral Measures and Scoring

Test of Visual Perceptual Skills-3rd Edition

The TVPS-3 is an assessment of visual perceptual strengths and weaknesses validated for individuals 4.0 years of age and older. The test uses black and white line drawings as stimuli for each of the seven subtests. Each item is administered in a multiple choice format. The seven subtests are administered in succession based upon difficulty level, starting with *Visual Discrimination* (a very basic visual skill) and ending with *Visual Closure* (a more advanced

Table 1 Means (SDs) of demographic and behavioral data

	Males (n=105)	Females (n=104)	Total Sample (n=209)	[∞] t (p)
Age	39.44 (10.28)	43.95 (12.42)	41.68 (11.59) Min: 19 Max: 69	*−2.86, p=0.005
BAP-Q				
Total average	3.20 (0.72)	2.98 (0.75)	3.09(0.74)	*2.16, p=0.032
Aloof	3.58 (1.09)	3.17 (1.09)	3.38(1.11)	*2.69, p=0.008
Pragmatic language	2.64 (0.78)	2.43 (0.82)	2.54(0.81)	1.76, p=0.080
Rigidity	3.37 (0.85)	3.37 (0.89)	3.37(0.87)	0.05, p=0.960
TVPS-3				
Figure-ground (scaled score)	8.79 (4.29)	8.27 (4.26)	8.54(4.30)	1.09, p=0.277
Reaction time (in seconds)	13.35 (8.27)	16.28 (11.98)	14.71(10.36)	*−2.06, p=0.04

[∞]T scores indicate results from group comparisons across BAP-Q scores, TVPS scores and reaction time between males and females. Significant differences between males and females ($p < 0.05$) are indicated (*) in the right column

visual skill). In a standard TVPS-3 administration, *Figure-Ground* is the sixth of the seven subtests to be administered. For the purposes of this study, *Figure-Ground* was the only TVPS-3 subtest administered and raw scores were converted to scaled scores using the TVPS-3 administration and scoring manual. Scaled scores for the TVPS-3 are transformed scores in which the distribution of raw scores have been fitted to a normal distribution with mean of 10 and standard deviation of 3. Although the TVPS-3 is normally untimed in the standard administration, we also obtained reaction time from the online administration (based upon the difference between when a stimulus was presented and a response via keyboard button press was provided). Average reaction time across all items for each participant was computed.

Broader Autism Phenotype Questionnaire

The (BAP-Q) (Hurley et al. 2007), is a self-report measure designed to assess subclinical, quantitative traits across core domains commonly used in characterizing the BAP (i.e. social aloof, rigidity and pragmatic language). Individuals are asked to rate how frequently each statement applies to them across a 6-point Likert scale ranging from very rarely to very often. Scores are averaged within each of the three subscales. Subscale scores are then averaged to produce an overall total score for each individual, a summary metric reflecting overall autism trait load across the three subscales. The BAPQ was originally derived from clinical assessment of parents with children with a diagnosis of ASD (Piven and Folstein 1994; Piven et al. 1997). In a validation against direct clinical assessment (Hurley et al. 2007) clinical cutoff scores were reported. Average total scores for our sample did not exceed clinical cutoffs on the BAPQ (Hurley et al. 2007) (≥ 3.35 for males; ≥ 3.25 for females).

Results

BAP-Q \times TVPS Relationship

We examined whether there is a relationship between quantitative measures of ALTs using the BAP-Q and individual differences in visual perceptual skills using the *Figure-Ground* subtest of the TVPS-3. Consistent with our hypothesis, a partial correlation of BAP-Q and *Figure-Ground* scaled scores controlling for age and gender revealed a significant relationship between TVPS- FG subtest scaled score and BAP-Q Aloof subscale score ($r=0.19$, $p=0.008$) Those participants with more ALTs in the BAPQ Aloof subscale were more accurate on the TVPS-FG subtest. TVPS-FG was not found to be related to BAP-Q Total

Average score ($r=0.09$, $p=0.21$, NS) or either of the other BAP-Q subscales (Rigidity: $r=0.04$, $p=0.57$, NS; Pragmatic Language: $r=0.02$, $p=0.75$, NS). There was no significant relationship between TVPS-FG reaction time and BAP-Q scores.

Gender differences (BAP-Q and TVPS)

We compared behavioral measures between males and females. BAP-Q Total Average scores were significantly higher for males compared to females ($t(207)=2.16$, $p=0.032$). In order to better understand whether scores within a particular domain of ALTs (Aloof, Pragmatic Language, or Rigidity) was influencing this difference, we examined differences between males and females across the three subscales of the BAP-Q. Male participants scored higher on the BAP-Q Aloof subscale relative to females ($t(207)=2.69$, $p=0.008$); however, there were no significant differences in BAP-Q Pragmatic Language ($t(207)=1.76$, $p=0.080$, NS) or BAP-Q Rigid ($t(207)=0.05$, $p=0.960$, NS) between males and females.

In addition to exploring gender differences in quantitative measures of autism traits, we compared TVPS *Figure-Ground* scores between males and females. We found no significant difference in *Figure-Ground* scaled scores ($t(207)=1.09$, $p=0.277$, NS). However, we found that male participants were significantly faster than female participants when comparing average reaction time on the TVPS FG subtest items ($t(207) = -2.06$, $p=0.04$).

Gender Differences in relationships between BAP-Q and TVPS

Given gender differences between the BAP-Q and TVPS, we next explored the relationship between ALTs and visual perceptual skills, separately for each gender. Within male participants, a partial correlation of BAP-Q and TVPS-FG scaled scores controlling for age revealed a significant relationship between TVPS-FG subtest scaled score and BAP-Q Aloof ($r=0.22$, $p=0.026$). Male participants with more ALTs as measured by the BAPQ Aloof subscale were more accurate on the TVPS-FG subtest. The relationship between the TVPS-FG subtest and BAP-Q Aloof was not present in females ($r=0.12$, $p=0.21$, NS).

There were no other significant relationships between TVPS-FG and BAP-Q measures within males [Total Average: $r=0.15$, $p=0.14$; Rigidity: $r=0.10$, $p=0.30$; Pragmatic Language: $r=0.03$, $p=0.79$, NS] or females [Total Average ($r=0.01$; $p=0.93$, NS); Aloof: $r=0.12$, $p=0.21$, NS; Pragmatic Language: $r=0.002$, $p=0.98$, NS; Rigidity: $r = -0.02$, $p=0.82$, NS]. There was also no significant relationship between TVPS-FG reaction time and BAP-Q scores for either males (p 's > 0.12) or females (p 's > 0.46).

Discussion

In the current study, we find a relationship between visuospatial processing and quantitative measures of autism features across the BAP. Additionally, the current study highlights important gender differences in the distribution of autism-like features and the relationship with visual perception in males relative to females. While the presence of heightened visual perceptual skills and enhanced local processing in individuals with ASD has been previously studied using the EFT, we made use of the Figure Ground subtest of the TVPS-3. Thus, this result differs from existing literature in 2 key ways. First, we show a continuous relationship between ALTs and visual perceptual skills, demonstrating that visual perceptual skills can be assessed along a continuum and scale with quantitative autism traits that extend beyond the diagnostic criteria for ASD. Common practice across studies of this phenomena in subclinical samples (i.e. those individuals without an ASD diagnosis) is to identify groups based upon “high” or “low” scores on an autism measure. Dichotomizing groups based upon relative scores fails to holistically capture the distribution of these traits across the general population. Secondly, we show a relationship between ALTs and the TVPS-FG subtest. Previous explanations of superior EFT performance in ASD have supported a framework of weak central coherence (WCC; Frith 1989; Frith and Happe 1994) which suggests a weakened ability to process global or contextual configurations in ASD (Happe and Frith 2006). More recent theoretical approaches, specifically the Enhanced Perceptual Functioning Model (Mottron et al. 2006; Samson et al. 2012), have suggested an enhanced engagement of sensory processing systems within ASD resulting in enhanced visual skills among other sensory and cognitive anomalies. While these tasks have proven effective in assessing disproportionate areas of strength in ASD, it was unclear whether this relationship was driven by the repetitive nature of the visual search task. The strength in using the TVPS-FG (as compared to the EFT) is its use of a unique target image and novel distractors on each trial. Thus, we have demonstrated that the repetitive visual search style associated with the EFT is not critical to assessing the link between visual perceptual ability and clinically relevant phenotypes.

One fundamental question is how visual perceptual anomalies are related to autism traits. Previous work has shown that an intact visual system is important for typical social development. For example, congenital blindness is thought to lead to increased levels of autism traits due to the impact of a deviant sensory experience on social development (Hobson et al. 1999; R Peter; Hobson and Bishop 2003; Jure et al. 2016). It is unclear whether atypical visual development in idiopathic autism leads to social deficits, specifically, or whether atypical visual perception is linked

broadly to a cumulative sum of autism traits or specific subdomain of atypical behaviors in autism. In our previous work, we have shown a linear relationship between atypical visual attention in autism and core social deficits during an inhibition of return paradigm (Antezana et al. 2016). Others have found correlations with overall autism traits (as opposed to subdomains of social or RRBs) in a visual task that measures attention to motion stimuli (Robertson et al. 2014, 2012). It has also been theorized that enhanced perceptual skill and hyperfocused states of attention are linked to the RRB domain, specifically circumscribed interests and resistance to disengagement (Landry and Bryson 2004; Sasson et al. 2011, 2008). From this perspective, the emergence of hyperfocused states of attention may simply be another manifestation of RRBs or potentially reflect a cognitive style that causes circumscribed interests to emerge. Here, we find a correlation between visual perceptual abilities and the BAP-Q Aloof subscale, which is thought to capture behaviors related to social motivation. Thus, we provide additional evidence of a specific link between social abilities and visual perception. Future work should continue to examine the impact of specific visual perceptual skills and their link to both broad and specific subdomains of autism traits.

Our results also highlight important gender differences in quantitative traits across the BAP as well as their relationships to measures of perceptual abilities. Females are more social than males, even early in infancy (Alexander and Wilcox 2012; Christov-Moore et al. 2014; Connellan et al. 2000; Hittelman and Dickes 1979). These gender differences also manifest in quantitative behavioral measures of autism traits (Baron-Cohen et al. 2001; Constantino 2011; Hiller et al. 2014). We chose to assess quantitative autism features using the BAP-Q and find higher overall ALTs as well as social aloof symptoms in our male cohort as compared to females. This aligns with previous studies that have made use of the BAP-Q and reported higher scores in males across all symptom domains (Davidson et al. 2014; Seidman et al. 2012). Importantly, most of the existing research using the BAPQ is based upon parents of children with an ASD diagnosis. Thus, our study offers important new knowledge with regard to the distribution of these traits in a broad sample.

In addition to gender differences in social traits, males displayed faster reaction times on TVPS-FG items but no differences in task performance, as well as a relationship between TVPS-FG and BAP-Q Aloof scores that was not significant in females. While there have been descriptions of differences in visual perception across males and females outside of ASD (Cairns et al. 1985; Hall et al. 1988; Huss and Kayson 1985), patterns of increased detail-focused attention has been observed in the BAP and particularly noted in fathers (as compared to mothers) of

children with ASD (Happé et al. 2001). Additionally, qualitative descriptions of the autism phenotype in females has highlighted unique social features relative to males that include increased awareness of and desire for social interaction in conjunction with better expressive behaviors (Lai et al. 2015) despite similarities in social processing deficits (Hiller et al. 2014). Thus, it is unclear whether atypical visual perception is truly only linked to social deficits and ALTs in males, or whether this is an artifact of gender differences in how social deficits manifest in behaviors.

The lack of a relationship between TVPS-FG and ALTs in females within the current context could be due to a variety of additional factors and warrants continued investigation within a controlled experimental setting. Previous findings have indicated gender differences in the use of cognitive compensatory strategies during tasks that require visual discrimination (Kimchi et al. 2009; McGivern et al. 1998) and have suggested that global interference impedes performance on tasks requiring local extraction. This would help elucidate why, within our sample, we identified differences in reaction time between males and females independent of differences in task performance. Females may have been taking longer and making use of alternative cognitive strategies as opposed to automatic perceptual strategies in order to complete the TVPS-FG subtest. The limitations of global relative to local processing biases and the modulating effects of a variety of factors (i.e. spatial frequency, visual angle, number and size of stimulus elements, stimulus content) have also been highlighted as potential reasons for discrepancies in reports of gender differences in visual perceptual skill (for reviews see Kimchi 1992; Navon 2003). The TVPS-3 includes six other subtests assessing various components of visual perception, ranging from very basic skills (visual discrimination) to more complex processes (visual memory). Future studies making use of the TVPS-3 in its entirety may highlight gender differences, specifically distinct components of perceptual strengths or strategies in females relative to males. Additional research utilizing a more comprehensive behavioral and experimental battery is warranted in order to fully characterize the gender differences in subclinical ALTs and the distinct relationships with visual perceptual skills between males and females.

In the current study, we do not show a relationship between RT and autism traits. This is in contrast to previous work that has demonstrated an effect of RT within visual paradigms (Grinter, Van Beek et al. 2009; O’Riordan 2004; O’Riordan et al. 2001; Plaisted et al. 1998; see; Cribb et al. 2016 for review), with evidence of faster RT and heightened performance in autism relative to controls. Within the current study, while RT was recorded and important gender differences in mean RT noted, we did not find significant relationships between

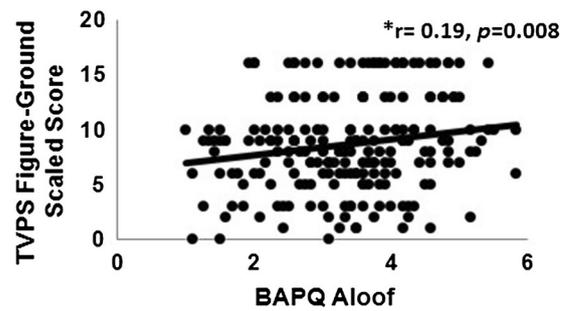


Fig. 1 Scatterplot depicting the relationship between TVPS-FG scaled scores and BAP-Q Aloof scores

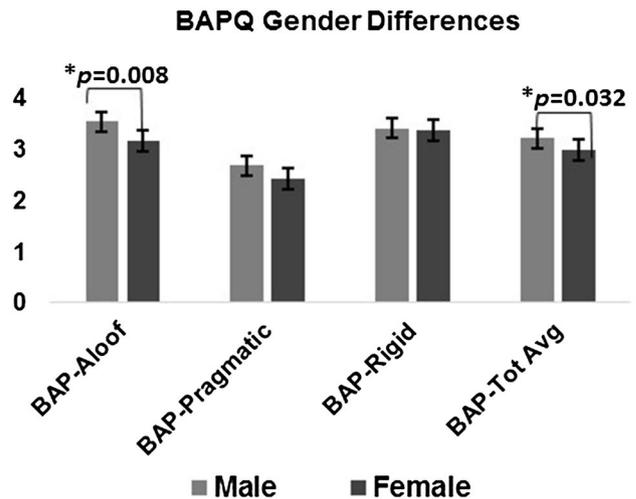


Fig. 2 Group-averaged (male and female) BAP-Q total average and subscale scores. Error bars reflect standard errors of the mean

RT and autistic features. Cribb et al. (2016) investigated individual differences in studies of visual perceptual performance in ASD using a quantitative measure of autism traits as both a continuous and quantile variable. While authors did report higher EFT performance in those who exhibited more autistic features, this effect was only seen when individuals were dichotomized based upon low versus high autistic traits. When studies used autistic traits as a continuous variable, similar to the approach of the current study, no relationship between autistic traits and EFT performance was observed. We may have not observed RT differences due to the use of the TVPS-3, as it is not a timed test and no time restraint was included in the current paradigm. The lack of a time limitation could have contributed to a high degree of variability in the time to make a response both within and between participants (see Table 1 for mean and st. devs.) that would have impacted our ability to detect significant results related to reaction time. A task without such temporal constraints,

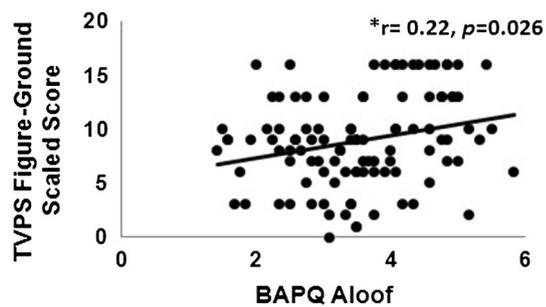


Fig. 3 Scatterplot depicting the relationship between TVPS-FG scaled scores and BAP-Q Aloof scores within our male cohort

granting participants an infinite amount of time to spend on each time, may have permitted individuals to make use of additional perceptual strategies to maximize performance. This is evident in ceiling effects on the TVPS-3 (see Figs. 1, 2, 3). Additionally, the repeated search for the same or similar targets within the EFT may facilitate faster RTs in the EFT in individuals with autism. The use of a different perceptual assessment with different task parameters may also contribute to reasons why no effect of RT was noted in the current study. Future research making use of the TVPS-3 and online data collection mechanisms such as those utilized here may want to step away from the formal TVPS-3 instruction and include timing restrictions in order to better assess the relationship between reaction time, task performance, and autistic features.

There are other limitations that should be considered in future studies. Despite the fact that reported results accounted for age and gender, our current sample includes a wide age range. Research has acknowledged the presence of age-associated cognitive decline, particularly across individuals ≥ 45 years of age (Levy 1994; Ritchie et al. 2001). In order to better quantify visual perceptual skill independent of age-related changes in cognition, future iterations of this work should focus on a more narrowed age range. Along the same lines, additional participant characteristics including developmental history, as well as diagnostic history should be collected in order to account for other variables potentially contributing to the relationship between atypical visual processing and relevant clinical traits. Despite these limitations, the current study contributes to a growing body of literature focused on the objective and dimensional measurement of quantitative traits across the BAP and their relationship to cognitive abilities.

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Author Contributions ASD and VT designed the research. ASD analyzed the data with guidance from VT. ASD and VT interpreted the data. ASD drafted the manuscript. ASD and VT critically revised the manuscript. All authors have read, reviewed, and approved the final version of the manuscript.

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Compliance with Ethical Standards

Conflict of interest The author A S DiCriscio and V Troiani declares that they have no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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