Neuropsychologia 63 (2014) 259–274

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Autism spectrum disorder, but not amygdala lesions, impairs social attention in visual search

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ARTICLE INFO

Article history:
Received 7 April 2014
Received in revised form
29 August 2014
Accepted 1 September 2014
Available online 8 September 2014

Keywords:
Visual search
Autism
Amygdala
Saliency
Social

ABSTRACT

People with autism spectrum disorders (ASD) have pervasive impairments in social interactions, a diagnostic component that may have its roots in atypical social motivation and attention. One of the brain structures implicated in the social abnormalities seen in ASD is the amygdala. To further characterize the impairment of people with ASD in social attention, and to explore the possible role of the amygdala, we employed a series of visual search tasks with both social (faces and people with different postures, emotions, ages, and genders) and non-social stimuli (e.g., electronics, food, and utensils). We first conducted trial-wise analyses of fixation properties and elucidated visual search mechanisms. We found that an attentional mechanism of initial orientation could explain the detection advantage of non-social targets. We then zoomed into fixation-wise analyses. We defined target-relevant effects as the difference in the percentage of fixations that fell on target-congruent vs. target-incongruent items in the array. In Experiment 1, we tested 8 high-functioning adults with ASD, 3 adults with focal bilateral amygdala lesions, and 19 controls. Controls rapidly oriented to target-congruent items and showed a strong and sustained preference for fixating them. Strikingly, people with ASD oriented significantly less and more slowly to target-congruent items, an attentional deficit especially with social targets. By contrast, patients with amygdala lesions performed indistinguishably from controls. In Experiment 2, we recruited a different sample of 13 people with ASD and 8 healthy controls, and tested them on the same search arrays but with all array items equalized for low-level saliency. The results replicated those of Experiment 1. In Experiment 3, we recruited 13 people with ASD, 8 healthy controls, 3 amygdala lesion patients and another group of 11 controls and tested them on a simpler array. Here our group effect for ASD strongly diminished and all four subject groups showed similar target-relevant effects. These findings argue for an attentional deficit in ASD that is disproportionate for social stimuli, cannot be explained by low-level visual properties of the stimuli, and is more severe with high-load top-down task demands. Furthermore, this deficit appears to be independent of the amygdala, and not evident from general social bias independent of the target-directed search.

1. Introduction

People with autism spectrum disorders (ASD) are characterized by pervasive impairments in social interaction and communication, together with restricted interests and repetitive behaviors (American Psychiatric Association, 2013). Laboratory-based measures reflecting the social impairments have documented abnormal eye tracking to social videos (Klin, Jones, Schultz, Volkmar, & Cohen, 2002) as well as static faces (Pelphrey et al., 2002). Work from our laboratory has argued for an increased tendency in adults with ASD to saccade away from the eye region of faces when information is present in those regions (Spezio, Adolphs, Hurley, & Piven, 2007b), and instead an increased preference to fixate the location of the mouth (Neumann, Spezio, Piven, & Adolphs, 2006), together with reliance of information from the mouth (Spezio, Adolphs, Hurley, & Piven, 2007a). Similarly, other eye tracking studies have found active avoidance of fixating the eyes in faces in people with ASD (Kliemann, Dziobek, Hatri, Steimke, & Heekeren, 2010). However, many other studies have shown normal social orienting and eye attention in people with ASD (see Guillon, Hadjikhani, Baduel, and Rogé, (2014) for a recent review); infants who later develop autism show an equally strong face orienting response (Elsabbagh et al., 2013) and adults with

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http://dx.doi.org/10.1016/j.neuropsychologia.2014.09.002
0028-3932/

ASD demonstrate a similar looking-time to faces as controls (Kuhn, Kourkoulou, & Leekam, 2010; Nakano et al., 2010). Young children with ASD show similar pattern of attention to the eyes and the mouth as typically developing controls (de Wit, Falck-Ytter, & von Hofsten, 2008; Falck-Ytter, Fernell, Gillberg, & Von Hofsten, 2010) and so do adolescents with ASD (McPartland, Webb, Keehn, & Dawson, 2011)—the story about reduced social orienting and eye attention in ASD is far from clear.

The findings showing abnormalities in how eyes are fixated by people with ASD may be related to the more subtle and heterogeneous findings in the literature regarding face processing. In particular, several studies have found reliable, but weak, deficits in the ability to recognize emotions from facial expressions (Kennedy & Adolphs, 2012; Law Smith, Montagne, Perrett, Gill, & Gallagher, 2010; Philip et al., 2010; Wallace et al., 2011) (for review, see Harms, Martin, and Wallace (2010)). The recognition of more complex mental states from faces may show a more reliable impairment in ASD, particularly if only the eye region of faces is shown (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001). Interestingly, abnormal fixations onto faces (Adolphs et al., 2005), abnormal recognition of emotion from facial expressions (Adolphs et al., 1999), and abnormal recognition of mental states from the eye region of faces (Adolphs, Baron-Cohen, & Tranel, 2002) have also all been reported in rare patients with amygdala lesions, providing some support for a long-standing hypothesis about the amygdala's involvement in ASD (Baron-Cohen et al., 2000).

Although there is evidence for global dysfunction at the level of the whole brain in ASD (Amaral, Schumann, & Nordahl, 2008; Anderson et al., 2011; Geschwind & Levitt, 2007; Piven et al., 1995), several studies emphasize abnormalities in the amygdala both morphometrically (Ecker et al., 2012) and in terms of functional connectivity (Gotts et al., 2012). Tying together the abnormal eye fixations onto faces in ASD mentioned above, and a correlation with amygdala processing, functional neuroimaging studies have found associations between abnormal fixation behavior and abnormal amygdala activation in people with ASD (Dalton et al., 2005; Kliemann, Dziobek, Hatri, Baudewig, & Heekeren, 2012). One recent study even found evidence for abnormal processing of information from the eye region of faces in single cells recorded from the amygdala in neurosurgical patients with ASD (Rutishauser et al., 2013). Despite considerable variability in reports of abnormal face processing in ASD, and despite the fact that there is brain dysfunction at a more global level in ASD, studies largely support (a) abnormal processing of faces in ASD, and (b) a link between this abnormality and amygdala function.

The human amygdala has been quite broadly implicated in processing emotionally salient and socially relevant stimuli (Adolphs, 2010; Kling & Brothers, 1992). Studies of a patient with bilateral amygdala lesions demonstrated a selective impairment in recognizing fearful faces (Adolphs, Tranel, Damasio, & Damasio, 1994), congruent with early neuroimaging studies (Morris et al., 1996). A distinctive aspect of our studies was the direct comparison between subjects with ASD, and rare patients with bilateral amygdala lesions.

Much of the work cited above has focused on abnormal social processing in ASD in relation to the features of faces. Yet it is clear that the impairment is broader than this: two-year-olds with autism orient to non-social contingencies rather than biological motion (Klin, Lin, Gorrindo, Ramsay, & Jones, 2009), and attention to pictures of people is reduced in relation to pictures that are non-social when these compete for visual attention (Sasson, Turner-Brown, Holtzclaw, Lam, & Bodfish, 2008; Sasson, Elison, Turner-Brown, Dichter, & Bodfish, 2011; Sasson & Touchstone, 2014). We capitalized on these prior findings, and used the stimuli developed in these prior studies, with slight modification (see *Methods* for further details). Notably, these images provided stimuli that fell into three categories: social, non-social, and special interest. The prior findings had shown, both in children and adolescents (Sasson et al., 2008), as well as in 2–5 year-olds (Sasson et al., 2011), that participants with ASD fixated social images less than controls when freely viewing the arrays. Our approach here extends this prior work in four important respects, with social attention defined as fixating and attending to social stimuli:

(1) We assessed high-functioning adults with ASD, and also manipulated the difficulty of our task (number of items in the array) to test whether abnormal social attention would be revealed even in high-functioning adults.
(2) We provided a comparison to a small sample (three) of subjects with bilateral amygdala lesions, to enable comparisons between these two populations in light of the prior findings we reviewed above.
(3) We modified the experiment so that all subjects were performing a uniform search task for either social or non-social targets (rather than free viewing).
(4) We added a control experiment that equates the items in the search array for low-level visual properties (standard saliency, size, and distance to center).

Visual search tasks are not new to autism research. Several studies have suggested superior visual search skills in individuals with ASD (Kemner, van Ewijk, van Engeland, & Hooge, 2008; Plaisted, O'Riordan, & Baron-Cohen, 1998; O'Riordan & Plaisted, 2001; O'Riordan, Plaisted, Driver, & Baron-Cohen, 2001; O'Riordan, 2004), particularly in relatively difficult tasks. Among various efforts to explain the differences, O'Riordan and Plaisted (2001) proposed two processing differences that could potentially explain the performance advantage: (1) enhanced memory for distractor locations already inspected, and (2) enhanced ability to discriminate between target and distractor stimulus features. Later, JJoseph, Keehn, Connolly, Wolfe, and Horowitz (2009) argued that the superiority is due to the anomalously enhanced perception of stimulus features.

While a sizable literature in ASD has investigated search for simple, non-social stimuli (shapes, letters, etc.) and only manipulated low-level attributes of the stimuli (Kemner et al., 2008; Manjaly et al., 2007; Plaisted et al., 1998; O'Riordan & Plaisted, 2001; O'Riordan et al., 2001; O'Riordan, 2004), far fewer studies have examined visual search with social stimuli. In the present study, we used a more general framework that does not restrict the stimuli to specific facial emotions, or investigate internal features of faces, but tests competition for attention between natural social (faces and people with various emotions and poses) and non-social (e.g., furniture, toys and food) stimuli when presented simultaneously in a search array. Given the reduced orientation towards social images in young children and adolescents with ASD when freely viewing the arrays (Sasson et al., 2008, 2011), we hypothesized that adults with ASD would have reduced attention to socially relevant items during visual search, while the deficits for attention to non-social items would be less pronounced. In a series of studies, we here explore whether the possible deficit depends on the amygdala (by comparisons with amygdala lesion patients tested on the identical tasks), and whether it depends on low-level visual properties of the search stimuli (by equating stimuli for their low-level visual properties in some of the studies). Since task demands such as the number of distractors can influence visual search performance (Lavie, Hirst, de Fockert, & Viding, 2004; Wolfe, 1998), we also test a variation of the search array with fewer distractors and test whether the possible deficit in ASD is disproportionate for higher cognitive loads (larger numbers of distractors), which would in turn suggest