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Brief social attention bias modification for children with autism spectrum disorder

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Lay Summary

Reduced looking at faces or eyes is an early feature for some individuals diagnosed with autism spectrum disorder (ASD). We tested whether a game, designed to increase attention to faces, could change visual attention in children diagnosed with ASD. Results suggest that children who played the game increased their visual attention to faces, suggesting that game-based methods to enhance looking at social stimuli may be a novel method to improve understanding of more complex social situations.

Abstract

Reduced social attention is a hallmark feature in autism spectrum disorder (ASD), emerging as early as the first year of life. This difference represents a possible mechanism impacting upon the development of more complex social-communicative behaviors. The aim of this study was to develop and test the efficacy of a novel attention bias modification paradigm to alter social attention, specifically orienting to faces. Children with ASD ($n = 66$), aged between 5-12 years, were randomized to play either a social attention training or control game for 15 minutes. Children playing the training game were reinforced for attending to and engaging with social characters, whereas children in the control group were equally rewarded for attending to both social and non-social characters. Eye-tracking measures were obtained before and after gameplay. There was a significant increase in the percentage of first fixations to faces, relative to objects, after social attention training compared to a control group, associated with a medium effect size (partial eta squared = .15). The degree of social attention change in the training group was inversely associated with restricted and repetitive behaviors and moderated by comorbid ADHD diagnoses, suggestive of differential training effects based on individual symptom profiles. By using the principles of attention bias modification, we demonstrated that social attention can be acutely modified in children with ASD, with an increased tendency to orient attention towards faces after brief social attention training. Modifying attentional biases may therefore represent a potential novel mechanism to alter the development of social-communication trajectories.

Keywords: social cognition, attention, eye movement

Introduction

Social attention refers to an innate human tendency to attend to socially relevant information (Birmingham & Kingstone, 2009). This social bias is evident early in life (Elsabbagh & Johnson, 2016) and is functionally significant for later social-communication development (Klin et al., 2002b; Leppänen & Nelson, 2009). Faces and eyes, in particular, are highly relevant biological stimuli, eliciting greater attentional preference and faster detection compared to non-face stimuli in children (Senju & Johnson, 2009b).

Reductions in visual social attention have been well-documented in individuals diagnosed with autism spectrum disorder (ASD) (Guillon et al., 2014), but are particularly evident at early stages of development, well before a diagnosis is made (Klin et al., 2002b; Maestro et al., 2002). For example, infants who have an older sibling diagnosed with ASD exhibit reduced attention to eyes between 2-6 months of age (Jones & Klin, 2013), reduced interest in faces at 6 and 9 months (Chawarska, Macari, & Shic, 2013), and exhibit slower ability to disengage from stimuli at 7 and 14 months (Elison et al., 2013; Elsabbagh et al., 2013). Reduced attention to the eye region of human faces also predicts severity of diagnostic symptoms in toddlers diagnosed with ASD (Jones, Carr, & Klin, 2008). As this bias manifests prior to the emergence of diagnostic behavioral symptoms, preferential orienting away from social information is a plausible underlying mechanism that may impact upon the development of social communication skills (Senju & Johnson, 2009a). This hypothesis suggests that difficulties or failures to engage with social information early in development cascade to impact upon the typical development of experience-dependent neural specialisations that support the onset of social-cognitive

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behaviors, such as shared joint attention or understanding emotion in others (Johnson et al., 2009; Schultz, 2005).

A large body of evidence supports the use of eye-tracking as a direct measure of visual attention as well as a quantifiable method for assessing subtle social phenotypes in ASD (Klin et al., 2002a). Using eye-tracking methods, the fundamental processes surrounding the allocation of social attention are altered in many individuals with ASD compared to non-ASD comparison samples (Chita-Tegmark, 2016; Guillon et al., 2014; Papagiannopoulou et al., 2014). Several studies suggest that children with ASD may not orient their attention to social stimuli (e.g. faces) when compared to non-social (e.g. objects) stimuli (see review in Chita-Tegmark, 2016). For example, using an attentional bias paradigm, which presents pairs of competing face and object images, Sasson and Touchstone (2014) demonstrated impaired initial orienting of gaze to social stimuli and reductions in the maintenance of attention to such stimuli in children with ASD. By contrast, Elsabbagh et al (2013) observed no impairment in initial orienting to social stimuli in response to a visual search “pop-out” paradigm.

A reduced orienting bias to social stimuli supports a more fundamental social preferencing difficulty, or gaze indifference, in ASD (Moriuchi et al., 2016). This social orienting hypothesis implies that, if social information is not visually prioritized, individuals with ASD may have difficulties learning the more complex nuances of social communication; ongoing difficulties in social behavior could then reflect the long-term effects of atypical orienting to social stimuli earlier in development (Klin et al., 2002b). It could then be speculated that any intervention targeting attentional allocation to social information could contribute to more general social and functional improvements.

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Whilst there is accumulating evidence for social attention biases in individuals with ASD, whether these can be modified acutely has not previously been tested. Given links between social attentional biases and social-communication traits, modifying attentional preferences to social information early in development could have the potential to alter social-communication trajectories. In the present study, we designed a game-based training paradigm, based on the principles of attention bias modification (Bar-Haim, 2010), to test whether social attention could be acutely modified. Attention bias modification paradigms are designed to encourage attention towards or away from a specific stimulus using simple paired stimuli contingencies. For example, these standalone training paradigms have exhibited efficacy in anxiety disorders by changing attention biases that maintain anxiety symptoms (Bar-Haim, 2010). Rather than targeting higher order social communication skills, we used attention bias modification principles to design and implement a social bias training paradigm for children with ASD to target the fundamental attentional processes underlying social communication difficulties. We then measured eye-gaze to social and non-social stimuli before and after playing this training game. We hypothesized that a single session of social attention training would directly increase attention to social stimuli when compared to children playing a control version. Specifically, we administered two social attention assessments immediately before and after training. The first, which provided the primary outcomes of interest, was an attentional bias task based on Sasson and Touchstone (2014). Here, we hypothesized that social attention training would increase initial orienting of gaze to social, relative to non-social, stimuli, and increase maintenance of attention (that is, total fixation time) towards social stimuli. We also included a secondary assessment of initial gaze orienting using a visual search task to compare training-related changes in initial

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orienting across the two tasks. However, given findings that similar visual search-based initial orienting may be intact in some children with ASD (Elsabbagh et al., 2013), we did not make any strong directional predictions with respect to this visual search task.

Method

Participants

We recruited children diagnosed with ASD, aged between 5 and 12 years ($n = 66$, 10 female). Formal diagnosis of ASD in Western Australia mandates consensus ratings by a multidisciplinary team comprising a paediatrician, clinical psychologist, and speech pathologist (Glasson et al., 2008). No exclusion criteria relating to cognitive function, language level, or comorbid conditions were applied. Diagnoses of intellectual disability, developmental delay, or medical/psychiatric comorbidities were obtained using parent-report. Comorbid diagnoses included attention deficit hyperactivity disorder (ADHD; $n = 19$), intellectual disability or global developmental delay ($n = 16$), and mood and/or anxiety disorders ($n = 7$). Two children had a known genetic mutation (22q.11 deletion). Reported current medication use included stimulants ($n = 12$), antipsychotics ($n = 5$), antidepressants ($n = 7$), and sleep medications ($n = 13$). Demographic characteristics of each group prior to exclusions for analyses are presented in Table S1 and final group demographic characteristics in Table 1. Written informed consent was provided by parents/caregivers and ethical approval was provided by the Human Research Ethics Committee at the University of Western Australia (RA/4/1/7350).

<insert Table 1 here>

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Measures

Clinical assessments: All children were administered the Autism Diagnostic Observation Schedule (ADOS-2; Lord et al., 2012) and either the Mullen Scales of Early Learning (MSEL; Mullen, 1995) or the Wechsler Intelligence Scale for Children (WISC-IV; Wechsler, 2003) to estimate developmental/cognitive functioning (using the Early Learning Composite score or full-scale IQ, respectively). Where an ADOS assessment had been conducted recently, this assessment was used. For children with older ADOS-Generic scores (Lord et al., 2012), assessments were re-scored to ADOS-2 algorithms. A comparison score was calculated that scales the overall total based on module, age, and/or overall expressive language level; higher scores indicate greater severity of symptoms.

Questionnaires: The Social Responsiveness Scale (SRS-2; Constantino & Gruber, 2012) and the Children's Communication Checklist (CCC-2; Bishop, 2003) were completed by a parent/carer at the time of assessment. These measure severity of social and communication difficulties, respectively, with scores normed relative to age (CCC-2) or gender (SRS-2). The CCC-2 is summed for a General Communication Composite (GCC) indicating severity of communication difficulties. The SRS-2 yields a total score as well as two DSM-5 subscales: Social-Communication and Restricted and Repetitive Behaviors (RRB); higher scores indicate greater severity.

Eye-tracking and game stimuli

Sets of social and non-social images were developed for the eye-tracking tasks and game. Social stimuli consisted of child and adult face stimuli (neutral, happy, angry,

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sad, and fear), obtained from the NIMH Child Emotional Faces Picture Set (Egger et al., 2011), the Karolinska Directed Emotional Faces (Lundqvist et al., 1998), and the NimStim Set of Facial Expressions (Tottenham et al., 2009), balanced for age, sex, and emotion. Non-social stimuli consisted of frequently endorsed circumscribed interests (for example, blocks, cars, trains, stimuli from popular contemporary computer games; Sasson, Turner-Brown, Holtzclaw, Lam, & Bodfish, 2008). A set of 60 social and 60 non-social images was used for the training paradigm and the visual search task (described below). A separate set of 20 social and 20 non-social images was used for the attentional bias assessment to demonstrate generalizability of training effects to new stimuli.

Social attention bias modification

The training paradigm, referred to as 'Frankie and Friends', was deployed using a Serious Game framework (Whyte et al., 2015) on a touchscreen tablet. The use of a touchscreen allowed for a more immersive experience suitable for children, with engaging visuotactile feedback based on swiping motions and sound effects.

Children were instructed to help 'Frankie', a cartoon dog, "find his friends". Several animated social and non-social characters, which displayed face or object images respectively, moved around the screen. Children earned points by selectively swiping the social characters (i.e. the faces) towards Frankie, while attempts to swipe a non-social character (i.e. the objects, such as toy dinosaurs, cars, trains) incurred a penalty. Training therefore encouraged preferential attention towards social information, and away from non-social information. Fifteen levels were created with increasing difficulty (increasing the minimum number of social characters that needed to be swiped towards Frankie to pass the level). If a child did not swipe

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enough characters in the allocated time (one minute), the level was restarted. Verbal prompting was used sparingly to encourage game completion. The control variant was identical in all features except for the critical training component. That is, children could earn points by swiping either social or non-social characters, rather than specifically social characters. For both training and control game variants, data were collected on the number and type of characters swiped as well as the time taken to pass each level. Children were randomized to a training condition prior to assessment using a predetermined block randomisation sequence.

Eye-tracking Procedures

Procedures followed general principles for eye-tracking in children diagnosed with ASD (Sasson & Elison, 2012). Children were seated comfortably in front of the eye-tracker and monitor at a viewing distance of 70 cm in a child-friendly sound-attenuated room with minimal distractions. A researcher sat beside and slightly behind the participant to encourage them to maintain attention and remain still. Eye-tracking data were collected using a Tobii X2-60 eye-tracker (60 Hz) mounted to the bottom frame of a 24-inch LCD monitor with 1920 x 1080 resolution. Gaze was recorded using an unobtrusive pupil centre corneal reflection technique, with approximately 0.5° accuracy for head movements within a 30 x 22 x 30 cm space. A 5-point infant calibration (a bouncing cat with sounds) was obtained prior to each task at each time point.

Two brief eye-tracking assessments were administered immediately before and after completion of the training game. Between trials, a three second video secured the initial locus of the child's gaze to the screen centre (e.g. image and sound of a deflating balloon).

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Attentional Bias (Sasson & Touchstone, 2014): this task provided our primary outcomes of initial orienting and attentional maintenance with social vs non-social stimuli; Figure 2A. Each trial consisted of a stimulus pair (social and non-social images), presented to the left and right of screen centre at an eccentricity of 9.76cm subtending at approximately 8° visual angle. Visual angle calculations have been based on the 70 cm viewing distance. Each image fit within a 15.86 x 15.86 cm square, subtending at a 13° visual angle. Stimulus pairs were presented in greyscale, luminance matched, and displayed for five seconds with a one second inter-trial interval. Social images were present with equal frequency to the left or right of the screen with 20 pre-randomized trials (see example stimuli in Figure S1). The dependent variable were the relative percentage of trials in which gaze was initially oriented (first fixation) to the social image (*attentional orienting*), as well as the average cumulative fixation time (the difference between social and non-social fixations averaged by number of valid trials; higher values indicative of greater social attentional bias); *attentional maintenance*.

Visual Search: this task provided a secondary measure of potential changes in initial gaze orienting to social vs non-social stimuli in response to visual “pop-out”. Forty trials were presented consisting of social and non-social visual arrays, in a similar format to the character arrays in the game. In social trials, one target social character was displayed amongst nine distractor non-social characters; in non-social trials, one non-social target was displayed with nine social distractors. Target and distractor locations varied randomly, with targets a minimum of 7.3 cm from screen centre, subtending at 6° visual angle, to necessitate saccadic orienting to the target. Stimuli were approximately 4.6x8.5 cm, subtending a visual angle of 3.8° by 6.9° (see example stimuli in Figure S2). Each array was presented for six seconds before

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a one second inter-trial interval, with 40 pre-randomized trials. For social and non-social arrays, the mean latency to initially fixate at the target stimulus was calculated, where lower values indicate greater attentional capture. A bias score was calculated (mean initial fixation latency for social targets minus mean initial fixation latency for non-social targets); higher scores reflecting greater social attention capture.

Data Analysis

Fixations were defined as gaze samples below a 30° per second velocity for a minimum duration of 100ms, using the Tobii Velocity-Threshold Identification algorithm (Tobii Technology, Danderyd, Sweden). For both tasks, trials were included if: (1) there were any fixation data recorded; (2) fixations were initially captured by the attention-getter at trial onset; and (3) the first saccade following trial stimulus onset occurred after 83ms, to remove anticipatory saccades.

Baseline differences between groups were compared using independent samples *t*-tests (two-tailed) and chi-square analyses (two-sided). Eye-tracking and game data were initially analysed with between-group ANOVAs for those children who played all 15 training levels and had sufficient gaze data on $\geq 25\%$ of trials in at least one of the two eye-tracking tasks. This resulted in 10 exclusions (training $n = 6$; control $n = 4$). Other missing data (incomplete eye-tracking data on one task, questionnaires, or clinical data) were excluded pairwise from analysis. Children excluded from analysis did not significantly differ on any demographic characteristic from those included; of those remaining, there were no significant differences between groups on any clinical, diagnostic, and cognitive measures (Table 1).

Pearson correlations were conducted between eye-tracking variables at baseline with demographic and clinical measures. Age, ADOS-2 severity, and WISC full scale

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IQs were significantly associated with quality of gaze recordings for the attention bias task, with age and IQ associated with quality of gaze during visual search (r 's ranging from $-.38$ to $.39$). This pattern suggested that older children with lower ASD severity and higher cognitive functioning were associated with better quality recordings. Although eye-tracking variables were calculated as a proportion of valid trials for each participant to account for individual variability in quality of recordings (Sasson & Elison, 2012), we re-analysed all eye-tracking outcomes using ANCOVAs, adjusting for age and ADOS-2 scores (full-scale IQ estimates were only available for 77% of the total sample, so were not included as a covariate). Significance was set at $p < .05$.

Results

Training data

Data collected during gameplay confirmed successful training; children playing the bias modification game selectively swiped social characters preferentially over objects (defined as the proportion of social characters selected as a function of overall characters selected), whereas children in the control group indiscriminately selected equal rates of both characters, $F(14, 756) = 6.38$, $p < .001$, $\eta_p^2 = .11$; see Figure 1. Pairwise comparisons confirmed increased proportion of social characters selected in the training group across all levels except the first (all p -values $< .001$; see Table S2, available online). As the control game was easier to acquire points and pass than the training game, children in the control group passed all levels except one significantly faster than children in the training group (all p 's $< .05$; see Table S2, available online).

<insert Figure 1 here>

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Eye-gaze changes

Attention Bias: A significant effect of training was observed in the percentage change of engagements (first fixations) to faces, associated with a medium effect size; $F(1, 47) = 8.15$, $p = .006$, $\eta_p^2 = .15$, adjusted for age and ADOS-2 severity. Children in the training group significantly increased the percentage of engagements to faces relative to objects after training (adjusted mean change = 17.24, SE = 7.16) compared to children in the control group (adjusted mean change = -12.87, SE = 7.60); see Figure 2B for unadjusted raw change scores. There were no significant differences in the change of overall fixation times to social and object stimuli, all p -values $> .05$ (see Table S3, available online).

<insert Figure 2 here>

Visual Search: An effect of time was observed for the time to fixate on incongruent stimuli, with faster speeds to find incongruent social stimuli relative to incongruent non-social stimuli at baseline, compared to after training, $F(1, 49) = 7.59$, $p = .008$, $\eta_p^2 = .13$. However, there was no significant effect between groups on the change from baseline in fixating on incongruent stimuli, after adjusting for age and severity scores, $F(1, 47) = 1.45$, $p = .23$, $\eta_p^2 = .03$.

Individual differences associated with training-induced eye-gaze changes

Exploratory correlations were run to examine any associations between the change in eye-gaze variables and clinical symptom measures (CCC-2, SRS-2, ADOS-2 severity). A significant overall association was observed for the SRS-2 total score

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and Social Communication subscale with changes in engagements to faces ($r = -.30$, $-.29$, respectively; $p < .05$), with a marginal trend for the RRB subscale ($r = -.26$, $p = .07$). When analysed by group separately, within the training group this association was only significant for the RRB subscale ($r = -.42$, $p < .05$) and a trend for the total score ($r = -.36$, $p = .07$); no significant association was observed in the control group. These findings suggested that children with a higher degree of change in engagement to faces after training were characterized by a reduced restricted interest and repetitive behavior profile; Figure 3.

<insert Figure 3 here>

As there was a significant proportion of children with an additional ADHD diagnosis, we conducted exploratory analyses to identify whether comorbid ADHD moderated training-induced changes in social attention. Between-groups analyses on social attention on both eye-tracking tasks were re-analysed with ADHD as a second between-subjects group factor. A significant interaction between training condition and ADHD diagnosis was observed on the change in percentage of engagements to faces; $F(1, 45) = 3.99$, $p = .05$, $\eta_p^2 = .08$, adjusted for autism severity and age. Follow-up pairwise comparisons indicated that the significant effect of training on first fixations to faces was only significant for children without ADHD (adjusted mean change = 42.18, SE = 11.83; $p = .001$) compared to children with ADHD (adjusted mean change = 1.92, SE = 18.63; $p = .92$). Re-analysis excluding children with ADHD (remaining sample: training $n = 20$, control $n = 17$) maintained the above significant effect of training in increasing first fixations to faces, although now this was associated with a large effect size; $F(1, 33) = 10.30$, $p = .003$, $\eta_p^2 =$

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.24; see Figure S3 for unadjusted raw change scores. This pattern of findings suggested that the degree of attentional change in engagement to faces after social attention training was moderated by presence of comorbid ADHD.

Discussion

The present study tested the efficacy of social attention bias modification in children with ASD, delivered through a novel game-based training paradigm. We first observed that active training, compared to a control variant, was successful in eliciting differential responding to social stimuli during gameplay, as assessed by the in-game metrics. Immediately following gameplay, active training led to increased orienting to social stimuli, associated with a medium effect size. The degree of orienting change was further associated with children's individual symptom profiles. No training effect was observed on attentional maintenance to social stimuli, suggesting that training was specific to an initial social engagement bias. These results indicate that brief social attention bias training increased initial engagement with faces, with greater changes in children with reduced autistic traits and without comorbid ADHD.

The findings provide the first evidence that a reduced social attention bias may be acutely modified in children with ASD through a single and brief training session. As the failure to engage with social information early in development may consequently alter developmental trajectories for social cognitive and communicative functioning (Chawarska et al., 2013; Falck-Ytter et al., 2013; Klin et al., 2002b; Maestro et al., 2002), it is pertinent to first establish whether such markers may indeed be modified. The present findings therefore provide a promising foundation for the prospective development of targeted technology-based training interventions in ASD.

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1
2 Interestingly, training appeared to selectively target the initial orienting of attention
3 with social stimuli, with no changes in the subsequent maintenance of attention. We
4 speculate that such findings are consistent with the structure of the game, whereby
5 efficient gameplay may encourage the rapid orienting of attention towards social
6 characters to score maximal points. While the findings are supportive of the capacity
7 to address impaired attentional orienting, it would now be optimal to also identify
8 methods of facilitating the maintenance of attention to social stimuli. Future research
9 may seek to identify variants of social attention bias modification that target
10 attentional maintenance to social information. It is also noted that the no training
11 related effects were evident for the visual search task. Given previous findings which
12 suggests that visual search based “pop-out” effects for social stimuli may be intact
13 for children with ASD (Elsabbagh et al., 2013), the findings are consistent with the
14 notion that the present training task may specifically target the initial orienting
15 impairments which have been shown to be associated with childhood ASD.

16
17 The design of the present study incorporates several methodological strengths.
18 First, the attentional training paradigm was developed from the bottom-up in
19 conjunction with ASD clinicians and children, within a Serious Game framework
20 (Whyte et al., 2015), thus creating a multifaceted gaming environment specifically
21 optimized for the engagement of children with ASD. We delivered the training using
22 an app-based platform based on the increasing interest in the use of technology-
23 based methods to improve social-communication skills in ASD (Wainer & Ingersoll,
24 2011). Technology-based interventions provide a medium through which skill
25 development can occur in a controlled, standardized, and predictable visuospatial
26 environment, while also enabling an individual to perform at their own pace and
27 ability (Golan & Baron-Cohen, 2006).

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While the present training task was developed for the purpose of modifying social attention bias, it is noted that the active and control training conditions not only differed in terms of attentional bias training, but also varied in terms of the requirement to respond to a goal-directed contingency. Given this, it is theoretically possible that the observed training effect may be alternatively accounted for by the differential training of attentional control (Browning, Holmes, Murphy, Goodwin, & Harmer, 2010; Chen, Clarke, Watson, MacLeod, & Guastella, 2015). Future research may seek to empirically test this notion by either examining for changes in attentional control, or by implementing a third training condition which requires goal-directed responding without social bias training (e.g. selective responding to shapes or colours). Future research should also seek to evaluate the clinical utility of social attention bias modification in ASD. While the findings of the current study are encouraging, it would be of central interest to determine whether repeated administration of this training task may lead to downstream changes in ASD-relevant symptomology. Lastly, the clinical and genetic heterogeneity within ASD is a significant challenge for hypothesis-driven treatment studies (Jeste & Geschwind, 2014). It is essential for research in this area to test individual symptom profiles as potential moderators of efficacy; the preliminary results from this study suggest that severity of RRB symptoms and presence of comorbid ADHD may moderate the effectiveness of social attention training in this group of children with ASD.

In conclusion, brief social attention bias modification has the potential to directly alter attentional orienting with social information in children with ASD. Findings from this study provide the first evidence to support the use of brief training-based paradigms to target fundamental attentional processing of social information in ASD. Future research will examine whether these changes in attentional bias can be

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maintained with extended training and whether effects may generalize to behavioral symptoms to alter social developmental trajectories.

References

- Bar-Haim, Y. (2010). Research review: attention bias modification (ABM): a novel treatment for anxiety disorders. *Journal of Child Psychology and Psychiatry*, 51(8), 859–870.
- Birmingham, E., & Kingstone, A. (2009). Human social attention. *Annals of the New York Academy of Sciences*, 1156(1), 118–140.
- Bishop, D. V. M. (2003). *The Children's Communication Checklist: CCC-2*. ASHA.
- Browning, M., Holmes, E. A., Murphy, S. E., Goodwin, G. M., & Harmer, C. J. (2010). Lateral prefrontal cortex mediates the cognitive modification of attentional bias. *Biological Psychiatry*, 67(10), 919–925.
- Chawarska, K., Macari, S., & Shic, F. (2013). Decreased spontaneous attention to social scenes in 6-month-old infants later diagnosed with autism spectrum disorders. *Biological Psychiatry*, 74(3), 195–203.
- Chen, N. T. M., Clarke, P. J. F., Watson, T. L., MacLeod, C., & Guastella, A. J. (2015). Attentional bias modification facilitates attentional control mechanisms: Evidence from eye tracking. *Biological Psychology*, 104, 139–146.
- Chita-Tegmark, M. (2016). Social attention in ASD: a review and meta-analysis of eye-tracking studies. *Research in Developmental Disabilities*, 48, 79–93.
- Constantino, J. N., & Gruber, C. P. (2012). *Social responsiveness scale (SRS) - 2nd edition*. California: WPS.
- Egger, H. L., Pine, D. S., Nelson, E., Leibenluft, E., Ernst, M., Towbin, K. E., & Angold, A. (2011). The NIMH Child Emotional Faces Picture Set (NIMH-CEFS): a new set of children's facial emotion stimuli. *International Journal of Methods in Psychiatric Research*, 20(3), 145–156.
- Elison, J. T., Paterson, S. J., Wolff, J. J., Reznick, J. S., Sasson, N. J., Gu, H., ...

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- 1
2
3 Evans, A. C. (2013). White matter microstructure and atypical visual orienting in
4
5 7-month-olds at risk for autism. *American Journal of Psychiatry*, 170(8), 899–
6
7 908.
8
9 Elsabbagh, M., Fernandes, J., Webb, S. J., Dawson, G., Charman, T., Johnson, M.
10
11 H., & Team, B. A. S. of I. S. (2013). Disengagement of visual attention in infancy
12
13 is associated with emerging autism in toddlerhood. *Biological Psychiatry*, 74(3),
14
15 189–194.
16
17 Elsabbagh, M., & Johnson, M. H. (2016). Autism and the social brain: the first-year
18
19 puzzle. *Biological Psychiatry*, 80(2), 94–99.
20
21 Falck-Ytter, T., von Hofsten, C., Gillberg, C., & Fernell, E. (2013). Visualization and
22
23 analysis of eye movement data from children with typical and atypical
24
25 development. *Journal of Autism and Developmental Disorders*, 43(10), 2249–
26
27 2258.
28
29
30
31 Glasson, E. J., MacDermott, S., Dixon, G., Cook, H., Chauvel, P., Maley-Berg, A., &
32
33 Wray, J. (2008). Management of assessments and diagnoses for children with
34
35 autism spectrum disorders: the Western Australian model. *Medical Journal of*
36
37 *Australia*, 188(5), 288.
38
39
40 Golan, O., & Baron-Cohen, S. (2006). Systemizing empathy: Teaching adults with
41
42 Asperger syndrome or high-functioning autism to recognize complex emotions
43
44 using interactive multimedia. *Development and Psychopathology*, 18(2), 591–
45
46 617.
47
48 Guillon, Q., Hadjikhani, N., Baduel, S., & Rogé, B. (2014). Visual social attention in
49
50 autism spectrum disorder: Insights from eye tracking studies. *Neuroscience &*
51
52 *Biobehavioral Reviews*, 42, 279–297.
53
54
55 Jeste, S. S., & Geschwind, D. H. (2014). Disentangling the heterogeneity of autism
56
57
58
59
60

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spectrum disorder through genetic findings. *Nature Reviews Neurology*, 10(2), 74–81.

Johnson, M. H., Grossmann, T., & Kadosh, K. C. (2009). Mapping functional brain development: Building a social brain through interactive specialization. *Developmental Psychology*, 45(1), 151.

Jones, W., Carr, K., & Klin, A. (2008). Absence of preferential looking to the eyes of approaching adults predicts level of social disability in 2-year-old toddlers with autism spectrum disorder. *Archives of General Psychiatry*, 65(8), 946–954.

Jones, W., & Klin, A. (2013). Attention to eyes is present but in decline in 2-6-month-old infants later diagnosed with autism. *Nature*, 504(7480), 427–431.

Klin, A., Jones, W., Schultz, R., Volkmar, F., & Cohen, D. (2002a). Defining and quantifying the social phenotype in autism. *American Journal of Psychiatry*, 159(6), 895–908.

Klin, A., Jones, W., Schultz, R., Volkmar, F., & Cohen, D. (2002b). Visual fixation patterns during viewing of naturalistic social situations as predictors of social competence in individuals with autism. *Archives of General Psychiatry*, 59(9), 809–816.

Leppänen, J. M., & Nelson, C. A. (2009). Tuning the developing brain to social signals of emotions. *Nature Reviews Neuroscience*, 10(1), 37–47.

Lord, C., DiLavore, P. C., & Gotham, K. (2012). *Autism diagnostic observation schedule*. Western Psychological Services Torrance, CA.

Lord, C., Rutter, M., DiLavore, P., Risi, S., Gotham, K., & Bishop, S. (2012). *Autism diagnostic observation schedule—2nd edition (ADOS-2)*. Los Angeles, CA.

Lundqvist, D., Flykt, A., & Öhman, A. (1998). The Karolinska directed emotional faces (KDEF). *CD ROM from Department of Clinical Neuroscience, Psychology*

Social attention modification & autism

Section, Karolinska Institutet.

Maestro, S., Muratori, F., Cavallaro, M. C., Pei, F., Stern, D., Golse, B., & Palacio-

Espasa, F. (2002). Attentional skills during the first 6 months of age in autism spectrum disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, 41(10), 1239–1245.

Moriuchi, J. M., Klin, A., & Jones, W. (2016). Mechanisms of diminished attention to eyes in autism. *American Journal of Psychiatry*, 174(1), 26–35.

Mullen, E. M. (1995). *Mullen scales of early learning*. AGS Circle Pines, MN.

Papagiannopoulou, E. A., Chitty, K. M., Hermens, D. F., Hickie, I. B., & Lagopoulos, J. (2014). A systematic review and meta-analysis of eye-tracking studies in children with autism spectrum disorders. *Social Neuroscience*, 9(6), 610–632.

Sasson, N. J., & Elison, J. T. (2012). Eye tracking young children with autism. *JoVE (Journal of Visualized Experiments)*, (61), e3675–e3675.

Sasson, N. J., & Touchstone, E. W. (2014). Visual attention to competing social and object images by preschool children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, 44(3), 584–592.

Sasson, N. J., Turner-Brown, L. M., Holtzclaw, T. N., Lam, K. S. L., & Bodfish, J. W. (2008). Children with autism demonstrate circumscribed attention during passive viewing of complex social and nonsocial picture arrays. *Autism Research*, 1(1), 31–42.

Schultz, R. T. (2005). Developmental deficits in social perception in autism: the role of the amygdala and fusiform face area. *International Journal of Developmental Neuroscience*, 23(2), 125–141.

Senju, A., & Johnson, M. H. (2009a). Atypical eye contact in autism: models, mechanisms and development. *Neuroscience & Biobehavioral Reviews*, 33(8),

Social attention modification & autism

1204–1214.

Senju, A., & Johnson, M. H. (2009b). The eye contact effect: mechanisms and development. *Trends in Cognitive Sciences*, 13(3), 127–134.

Tottenham, N., Tanaka, J. W., Leon, A. C., McCarry, T., Nurse, M., Hare, T. A., ... Nelson, C. (2009). The NimStim set of facial expressions: judgments from untrained research participants. *Psychiatry Research*, 168(3), 242–249.

Wainer, A. L., & Ingersoll, B. R. (2011). The use of innovative computer technology for teaching social communication to individuals with autism spectrum disorders. *Research in Autism Spectrum Disorders*, 5(1), 96–107.

Wechsler, D. (2003). Wechsler intelligence scale for children—Fourth Edition (WISC-IV). *San Antonio, TX: The Psychological Corporation*.

Whyte, E. M., Smyth, J. M., & Scherf, K. S. (2015). Designing serious game interventions for individuals with autism. *Journal of Autism and Developmental Disorders*, 45(12), 3820–3831.

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Table*Table 1.* Baseline characteristics.

	Training <i>N</i> = 28	Control <i>N</i> = 28	
	Mean (SD), Range	Mean (SD), Range	<i>p</i> value ¶
Chronological age, months	106.36 (25.29), 59-145	100.29 (27.94), 61-153	.40
Age at diagnosis, months	54.43 (26.11), 18-132	54.46 (24.02), 24-120	1.00
ADOS-2, comparison score	5.43 (2.03), 2-10	4.79 (1.85), 2-9	.22
MSEL, composite score †	76.20 (21.66), 55-102	85.25 (16.78), 63-105	.41
WISC, full-scale IQ ‡	87.35 (17.56), 65-108	90.10 (12.97), 65-108	.57
CCC-2, communication composite §	33.63 (13.45), 11-67	34.26 (11.27), 9-58	.89
SRS-2, total T-score §	74.89 (9.85), 58-90	78.61 (9.62), 63-90	.16
	<i>N</i> (%)	<i>N</i> (%)	<i>p</i> value ¶¶
Male / Female	22 (78.6) / 6 (21.4)	26 (92.9) / 2 (7.1)	.13
Comorbid conditions:			
Intellectual disability / developmental delay	8 (28.6)	8 (28.6)	1.00
ADHD	5 (17.9)	7 (25.0)	.52
Mood / Anxiety Disorders	3 (10.7)	3 (10.7)	1.00

Note. Baseline characteristics of children included in analyses of game and eye-tracking data after exclusions made for poor quality gaze data and/or insufficient gameplay of all levels. † Training *N* = 5, Control *N* = 8; ‡ Training *N* = 23, Control *N* = 20; § Training *N* = 27, Control *N* = 28; ¶ Independent samples *t*-test; ¶¶ Chi-square test.

Abbreviations: Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2), Mullen Scales of Early Learning (MSEL), Wechsler Intelligence Scale for Children, 4th edition (WISC-IV), Children's Communication Checklist, 2nd edition (CCC-2),

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Social Responsiveness Scale, 2nd edition (SRS-2), Attention Deficit Hyperactivity Disorder (ADHD).

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Figure Captions

Figure 1. Proportion of social characters selected during gameplay across 15 levels.

Note. Significant interaction between training condition and time, $F(14, 756) = 6.38$, $p < .001$, partial $\eta^2 = .11$. Pairwise comparisons indicated a significant difference between conditions for all levels at $p < .001$ except the first level. Error bars represent standard deviation.

Figure 2. Effects of social attention bias training on initial fixations to faces.

Note. (A) Example of eye-tracking stimulus; (B) Changes in proportion of first fixations to faces after training (unadjusted change scores). A significant effect of training group was observed in increased orienting towards faces, relative to objects, compared to the control group. Error bars represent standard deviations.

Figure 3. Associations between training-induced changes in first fixations to faces with the Social Responsiveness Scale (SRS-).

Note. (A) SRS- total score, Training $r = -.36$, $p = .07$, Control $r = -.06$, $p = .79$; (B) SRS- Social Communication subscale, Training $r = -.31$, $p = .12$, Control $r = -.09$, $p = .68$; (C) SRS- Restricted Repetitive Behavior subscale, Training $r = -.42$, $p = .03$, Control $r = .02$, $p = .93$. Training $N = 26$, Control $N = 24$. Error bars represent 95% confidence intervals.

Figure 1. Proportion of social characters selected during gameplay across 15 levels.

Note. Significant interaction between training condition and time, $F(14, 756) = 6.38$, $p < .001$, partial $\eta^2 = .11$. Pairwise comparisons indicated a significant difference between conditions for all levels at $p < .001$ except the first level. Error bars represent standard deviation.

73x53mm (600 x 600 DPI)

Figure 2. Effects of social attention bias training on initial fixations to faces. Note. (A) Example of eye-tracking stimulus; (B) Changes in proportions of first fixations to faces after training (unadjusted change scores). A significant effect of training group was observed in increased engagements towards faces, relative to objects, compared to the control group. Error bars represent standard deviations

122x147mm (300 x 300 DPI)

Figure 3. Associations between training-induced changes in first fixations to faces with the Social Responsiveness Scale (SRS-2).

Note. (A) SRS-2 total score, Training $r = -.36, p = .07$, Control $r = -.06, p = .79$; (B) SRS-2 Social Communication subscale, Training $r = -.31, p = .12$, Control $r = -.09, p = .68$; (C) SRS-2 Restricted Repetitive Behavior subscale, Training $r = -.42, p = .03$, Control $r = .02, p = .93$. Training $N = 26$, Control $N = 24$. Error bars represent 95% confidence intervals.

170x346mm (300 x 300 DPI)

Method

Examples of eye-tracking stimuli

Attentional Bias: social (face) and non-social (circumscribed interest) stimuli were paired based on methods described in Sasson and Touchstone (2014), using exemplars from five categories (trains, vehicles, airplanes, clocks and blocks) and five emotional categories (happy, sad, angry, fearful, neutral). Images were sized to match in area and were luminance matched by converting images to greyscale.

Figure S1. Example images from the attentional bias task. (A) a happy adult face is paired on the right with a train on the left. (B) a fearful adult face is paired on the left with a clock on the right.

Visual Search: visual arrays of images were created to mimic the format of the game display. In each array, a set of nine social (or non-social) distractor stimuli were presented with one target non-social (or social) stimuli from the opposite class of stimuli. Locations of targets and distractor stimuli varied between trials.

Figure S2. Example images from the visual search task. (A) a happy adult face target stimuli is located on the far right upper corner with nine distractor non-social stimuli. (B) a clock target stimuli is located in the far right upper corner with nine face distractor stimuli.

Table S1. Baseline characteristics of entire sample.

	Training N=34	Control N=32	p value
	Mean (SD), Range	Mean (SD), Range	¶
Chronological age, months	106.03 (24.42), 59-145	96.53 (28.09), 60-153	.15
Age at diagnosis, months	57.65 (26.80), 18-132	52.91 (22.90), 24-120	.44
ADOS-2, comparison score	5.26 (1.99), 2-10	5.06 (2.00), 2-10	.68
MSEL, composite score †	80.33 (21.86), 55-102	78.64 (19.40), 49-105	.87
WISC, full-scale IQ ‡	86.19 (17.67), 50-118	90.62 (12.86), 65-108	.34
CCC-2, communication composite §	33.72 (12.54), 11-67	34.42 (10.82), 9-58	.81
SRS-2, total T-score §	75.67 (9.65), 58-90	77.68 (9.72), 62-90	.41
	N (%)	N	p value
			¶¶
Male / Female	27 (79.4)	29 (90.6)	.20
Comorbid conditions:			
Intellectual disability / developmental delay	11 (32.4)	6 (18.8)	.21
ADHD	11 (32.4)	8 (25.0)	.51
Mood / Anxiety Disorders	4 (11.6)	3 (9.4)	.75

Note. Baseline characteristics of all children recruited for the study.

† Training N=6, Control N=11; ‡ Training N=27, Control N=21; IQ estimates missing for 2 minimally verbal children in the training group; § 3 and 2 questionnaires missing for the CCC-2 and SRS-2, respectively, for minimally verbal children; ¶ Independent samples *t*-test; ¶¶ Chi-square test.

Abbreviations. Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2); Mullen Scale of Early Learning Developmental Quotient (MSEL); Wechsler Intelligence Scale for Children (WISC); Children's Communication Checklist-2 (CCC-2); Social Responsiveness Scale-2 (SRS-2); Attention Deficit Hyperactivity Disorder (ADHD).

Table S2. Number of Characters Selected and Time to Complete Level

	Social Characters Selected				Non-Social Characters Selected				Time to Complete Level †			
	Training		Control		Training		Control		Training		Control	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Level 1	15.07	7.54	16.82	9.60	9.86	14.20	12.93	12.63	40.51	11.83	32.55	10.70
Level 2	22.39	7.69	27.29	13.08	5.36	7.67	25.50	17.05	31.22	12.10	16.85	6.84
Level 3	24.11	6.31	27.82	13.81	6.36	11.12	25.93	17.40	30.52	9.38	18.28	12.57
Level 4	27.71	9.70	28.64	12.08	5.89	10.64	23.36	15.24	36.11	8.31	24.36	10.31
Level 5	29.21	9.94	27.18	12.85	5.14	10.12	25.54	14.33	38.14	10.24	26.84	11.43
Level 6	31.11	8.94	28.25	13.20	4.14	4.87	24.29	15.86	36.36	7.56	28.41	14.02
Level 7	40.57	16.05	32.18	14.69	3.71	2.69	27.79	14.90	37.49	7.28	29.82	10.10
Level 8	42.21	15.90	30.54	16.69	3.14	1.80	26.57	16.61	37.17	7.50	32.52	12.10
Level 9	44.00	17.34	33.46	13.52	3.89	2.81	26.86	14.49	38.71	10.18	29.59	10.66
Level 10	42.93	16.63	32.82	13.19	3.79	2.94	29.75	12.29	39.01	8.32	30.85	11.18
Level 11	44.32	17.27	31.29	13.21	4.39	3.75	31.64	14.39	39.39	10.55	32.34	12.67
Level 12	45.57	15.39	32.50	14.69	5.04	4.19	31.71	13.54	38.91	9.53	30.02	11.31
Level 13	44.39	16.32	33.64	13.80	4.46	4.16	32.18	14.14	41.19	9.73	29.31	9.10
Level 14	44.29	17.98	33.32	12.89	4.39	4.20	30.43	14.68	38.38	9.71	29.34	10.71
Level 15	45.25	15.41	34.57	15.74	4.39	3.39	31.75	14.60	39.96	9.77	29.83	11.06

Note. Training $N=28$, Control $N=28$. † Time indicates the number of seconds at which the minimum number of characters required to pass the level was achieved (10 characters on first levels up to 30 characters on final levels). Levels increased in difficulty (more characters needed to pass level, characters decreased in size and moved faster on screen) to encourage continued engagement. After passing a level, children were encouraged to keep swiping characters to get a 'top score' to ensure all children received a standard 15 minutes of training. As not all children reached the minimum number of characters for each level (and thus no time data was recorded for that level), the number of participants included in each 'Time to Complete Level' cell differs across each level (total N ranges from 43–54). All levels were passed significantly faster in the control group (all p 's < .05), except for level 8.

Table S3. Unadjusted means and standard deviations for pre- and post-training eye-tracking variables

Attention Bias	Pre				Post				Interaction <i>p</i> -value †	η_p^2
	Training <i>N</i> =27		Control <i>N</i> =24		Training <i>N</i> =27		Control <i>N</i> =24			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
First fixations to faces, %	42.57	23.81	54.75	19.91	50.68	26.95	48.90	20.35	.01	.13
Fixation time to faces, ms	1384.04	412.56	1327.15	505.51	1283.92	703.84	1279.78	557.43	.75	.00
Fixation time to objects, ms	1597.97	385.91	1674.04	392.43	1392.01	499.91	1657.05	541.12	.16	.04
Visual Search	Pre				Post				Interaction <i>p</i> -value †	η_p^2
	Training <i>N</i> =26		Control <i>N</i> =25		Training <i>N</i> =26		Control <i>N</i> =25			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Latency to locate face, ms	1162.63	367.18	1298.61	406.56	1538.96	996.32	1395.77	660.98	.26	.03
Latency to locate object, ms	2105.411	825.03	2349.57	600.70	1830.37	1146.77	2196.77	1147.21	.74	.00

Note. † Mixed ANOVA with group (training, control) as the between-subjects factor and time (pre, post) as the within-subjects factor. No adjustments made for chronological age or severity. Adjustments for these covariates did not change interpretation of the above.

Figure S3. Effects of social attention bias training on initial fixations to faces is moderated by ADHD diagnosis.

Note. Raw unadjusted change scores. Pairwise comparisons confirmed a significant difference between training and control conditions for children without a comorbid ADHD diagnosis, $p = .002$ (mean difference between conditions = 38.37, SE = 11.48), which was not observed in children with ADHD, $p = .92$ (mean difference between conditions = 1.98, SE = 18.61). Error bars represent standard deviations.