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ORIGINAL PAPER

Applying Eye Tracking to Identify Autism Spectrum Disorder in Children

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Abstract

Eye tracking (ET) holds potential for the early detection of autism spectrum disorder (ASD). To overcome the difficulties of working with young children, developing a short and informative paradigm is crucial for ET. We investigated the fixation times of 37 ASD and 37 typically developing (TD) children ages 4–6 watching a 10-second video of a female speaking. ASD children showed significant reductions in fixation time at six areas of interest. Furthermore, discriminant analysis revealed fixation times at the mouth and body could significantly discriminate ASD from TD with a classification accuracy of 85.1%, sensitivity of 86.5%, and specificity of 83.8%. Our study suggests that a short video clip may provide enough information to distinguish ASD from TD children.

Keywords Autism · Eye tracking · Fixation time · Machine learning · Face

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder that affects more than 1% of children and is defined by deficits in social interaction and communication, as well as restricted and repetitive patterns of behavior. The etiology and pathophysiology of ASD remain unclear. Although no cure currently exists, multidimensional and multidisciplinary interventions (behavioral approaches, biomedical agents, and alternative medicine) have been applied to improve the quality of life of individuals with ASD. Moreover, many such interventions have been deemed effective (Lai et al. 2014; Sharma et al. 2018). Accumulating evidence suggests that early diagnosis and intervention can significantly impact the prognosis of individuals with ASD as well as reduce societal costs (Lai et al. 2014; Zwaigenbaum and Penner 2018).

Due to complexity, heterogeneity, and chronogeneity of ASD, clinical guidance documents generally recommend that multidisciplinary teams are involved in the diagnosis of ASD (Zwaigenbaum and Penner 2018). Of the various diagnostic tools available, the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview—Revised (ADI-R) display the highest sensitivity and specificity (Falkmer et al. 2013; Zwaigenbaum and Penner 2018). Although these tools are powerful in identifying behaviors related to ASD, many users have noted issues in their "diagnostic discrimination and required resources" (Akshoomoff et al. 2006; Lai et al. 2014). More specifically, usage of ADOS and ADI-R tends to be associated with substantial time costs and can lead to overdiagnosis of ASD (Akshoomoff et al. 2006).

To improve such issues, easier, faster, and more objective screening methods, especially for younger children, are urgently needed (Bolte et al. 2016; Elsabbagh and Johnson 2016). In recent decades, a number of biomarkers have

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earned merit in their ability to identify individuals who are at high risk for developing ASD (Zwaigenbaum and Penner 2018). Such biomarkers assess genetic variation, early brain structural and functional connectivity, visual orienting, and other biological processes prior to the onset of the disorder's more characteristic behavioral symptoms (Zwaigenbaum and Penner 2018).

One emerging objective tool increasingly being applied in ASD clinics and research is eye tracking (ET) (Falck-Ytter et al. 2013). As a non-invasive and convenient measurement, ET uses relatively objective parameters to avoid the possibility of bias that is found in traditional subjective evaluations caused by asymmetric information between patients (or parents) and examiners (Zwaigenbaum and Penner 2018).

Avoiding a person's eyes or face is a unique gaze fixation pattern in ASD (Fujioka et al. 2016). Therefore, measurements of eye movements using ET technology have been widely applied in ASD research, significantly improving our understanding of gaze patterns in the ASD population. The most frequently used ET paradigm involves videos or photographs of human faces (Annaz et al. 2012; Chawarska and Shic 2009; Dalton et al. 2005; Fujisawa et al. 2014; Jones et al. 2008; Klin et al. 2009; Shic et al. 2014; Speer et al. 2007; Sterling et al. 2008). Studies applying this paradigm have detected gaze abnormalities in individuals with ASD. These studies found that compared with age-matched typically developing (TD) children, children with ASD spent less time gazing at eyes and faces and tended to look at irrelevant targets (Falck-Ytter et al. 2012). These findings are not only consistent with clinical observations of ASD but also provide new insights for the early detection of ASD.

In a previous study, investigators investigated gaze duration on a face using a paradigm in which they presented a female face (1) still, (2) moving and expressing positive affect, and (3) speaking. They compared gaze durations of 6-month-old infants with ASD at different regions of the face. The results showed that the duration of gaze at the inner facial features decreased compared with other groups only when the presented face was speaking (Shic et al. 2014), indicating that a speaking face may be more useful for distinguishing ASD from TD children.

Recently, a machine learning method has been applied to distinguish individuals with ASD from those without ASD and has demonstrated great potential. As a subset of artificial intelligence in the field of computer science, machine learning is a procedure that trains a computer algorithm to analyze a set of observed data and statistically learn the latent patterns without being explicitly programmed. It has been applied on behavior (Crippa et al. 2015; Kosmicki et al. 2015), brain activity (Deshpande et al. 2013), and ET (Liu et al. 2016), and it has achieved encouraging results.

Although the aforementioned studies have demonstrated the potentials of eye tracking, one challenge that remains is the cooperation of participants, particularly infants and young children, with whom ET holds the greatest potential for early detection. It is difficult to keep such subjects focused on a monitor for a long time. Thus, the screening paradigm applied should not only be informative, but also short.

In this preliminary study, we recruited a cohort of 4–6 year-old children with ASD and a cohort of age- and gender-matched TD children. We presented a 10 s muted video clip of a female speaking to investigate gaze fixation time on different areas of the female's face using a method applied in a previous study (Shic et al. 2014). There were two aims in this preliminary study: (1) replicating the findings observed in previous research using a population of different ages (6 months vs 4–6 years old) and (2) extending the previous findings by exploring which part of the face could be used to distinguish ASD from TD children using a machine learning method.

Materials and Methods

Participants

Participants in the ASD group were recruited from an outpatient ward of the Child Mental Health and Rehabilitation Center at the Shenzhen Maternity & Child Healthcare Hospital in China. Inclusion criteria were: (1) aged 4–6 years, and (2) Childhood Autism Rating Scale (CARS) score greater than 30, in line with the ADOS standard. Due to the limited access to the ADI-R and ADOS in China, all diagnoses were made by experienced physicians based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and CARS score. In addition, the Gesell Developmental Scale (GDS) (Chinese version) (Zhang et al. 1994) was applied to explore the association between the eye tracking measurement and behavioral/clinical outcomes.

TD children were recruited as controls from a kindergarten in the same city. Prior to their recruitment, the control participants were screened by a licensed physician to exclude anyone with a history of psychiatric or neurological disorders, including ASD.

The present research has been approved by the Ethics Committee of the Shenzhen Maternity & Child Healthcare Hospital, and all parents provided informed consent prior to subject enrollment.

Experimental Stimuli

We used the SMI RED250 portable ET system in this study. After five-point calibration, a silent video of a young Asian female mouthing the English alphabet was presented for 10 s (Kong et al. 2017). The screen resolution was set to

1024 × 768 pixels with a sampling frequency of 250 Hz and spatial resolution of 0.03°.

Procedure

Children were seated in front of a 22 inch widescreen LCD monitor in a dark and soundproof room. The center of their vision was aligned with the center of the monitor, with an eye-to-monitor distance of 65 cm. Before the short video presentation, eye position correction was performed by having the subjects fixate on a dynamic pink rabbit. After this, the stimulus described was presented. Gaze patterns were recorded on a BeGaze data analysis software system.

Analytic Strategy

Areas-of-Interest

The following ten areas-of-interest (AOI) were examined: (1) background; (2) body: neck, shoulders, and chest; (3) hair; (4) outer-face: the face area excluding the mouth, nose and eyes; (5) eyes; (6) nose; (7) mouth; (8) person: hair, body, face; (9) face: outer-face, eyes, nose, and mouth; (10) outer-person: hair and body (Fig. 1).

Similar to a previous study (Shic et al. 2014), we defined several ratios to adjust for the generally low fixation time of ASD children. These ratios include: (1) eyes-to-face ratio: eyes fixation time/face fixation time; (2) nose-to-face ratio: nose fixation time/face fixation time; (3) mouth-to-face ratio: mouth fixation time/face fixation time.

Statistical Analysis

Data analyses was processed with SPSS 22.0 (SPSS Inc., Chicago, Illinois, USA). Sociodemographic data and AOI fixation time between the ASD and TD groups were analyzed using two independent sample t tests and χ^2. Bonferroni correction was used to adjust the p-value for multiple comparisons.

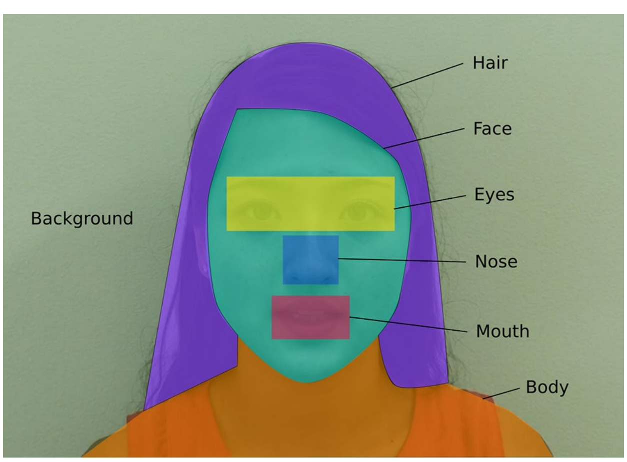

Fig. 1 AOI overlaid on human face

Discriminant Analysis

To explore whether any AOIs could discriminate ASD from TD, we applied machine learning with support vector machine (SVM) on fixation time using five-fold cross validation. The discriminative weights of the AOIs, which indexed the importance of fixation time at each AOI in discriminating ASD from TD, were statistically assessed using permutation tests (1000 times with the null hypothesis that the value of weights was arbitrary) to determine the reliability of each AOI in discrimination.

Discriminant analysis performance was assessed by accuracy, sensitivity, and specificity. To determine whether the classification performance was significantly better than chance level, we permuted the labels of children and estimated location of the real accuracy within the distribution of all permuted accuracies (1000 times).

Results

In this study, there was a total of 37 ASD children and 37 age- and gender-matched TD children. There was no significant difference in age or gender between the two groups (Table 1).

Participants' Fixation Times at AOIs

Analysis of the ten AOIs showed that the fixation times at the eyes, mouth, nose, body, person, face, and outer-person were all significantly lower in the ASD group compared to

Table 1 Demographic and clinical traits for all participants (mean ± SD)

Characteristic	ASD (n = 37)	TD (n = 37)	p value
Age	4.6 ± 0.7	4.8 ± 0.4	0.17
Gender (boys/girls)	33/4	27/10	0.14*
CARS score	34.4 ± 7.8	–	–
GDS score			
Adaptation score	62.8 ± 15.0	–	–
Large motion score	73.7 ± 11.1	–	–
Fine motion score	59.2 ± 15.5	–	–
Language score	46.9 ± 15.2	–	–
Personal-social score	53.5 ± 10.7	–	–

*The p value was obtained by χ^2 test; other p values were obtained by a two-independent sample t test

CARS Childhood Autism Rating Scale, *GDS* Gesell Developmental Scale the TD group ($p < 0.005$, 0.05/10 after Bonferroni correction) (Fig. 2). In addition, we explored the ratio differences between the two groups and found no significant differences in the eyes-to-face ratio ($p = 0.39$), mouth-to-face ratio ($p = 0.95$), or nose-to-face ratio ($p = 0.87$).

To further explore the association between gaze fixation and behavioral outcomes in ASD children, we also applied a partial correlation between total fixation times with significant group differences and social, emotional, and adaptive subscores of the GDS, including age and gender as covariates. We found a significant association between fixation time and large motion subscore in ASD children ($p < 0.01$, 0.05/5 after Bonferroni correction). In addition, ASD groups also showed a correlation trend between fixation time and adaptation ($p = 0.03$, not significant after Bonferroni correction), language ($p = 0.03$), and personal-social ($p = 0.04$) subscores.

Discriminant Analysis

Among the AOIs, discriminant analysis showed that fixation time for the body and mouth could significantly discriminate ASD from TD ($p = 0.03$ and $p = 0.008$, respectively). Classification accuracy was 85.1%, sensitivity was 86.5% (the proportion of ASD individuals correctly classified), and specificity was 83.8% (the proportion of TD individuals correctly classified). Permutation tests revealed that the classification accuracy was significantly higher than chance level ($p < 0.001$).

Discussion

In this proof of concept study, we investigated fixation time on different areas of a female face that was speaking among 4–6 year-old Asian children with and without ASD.

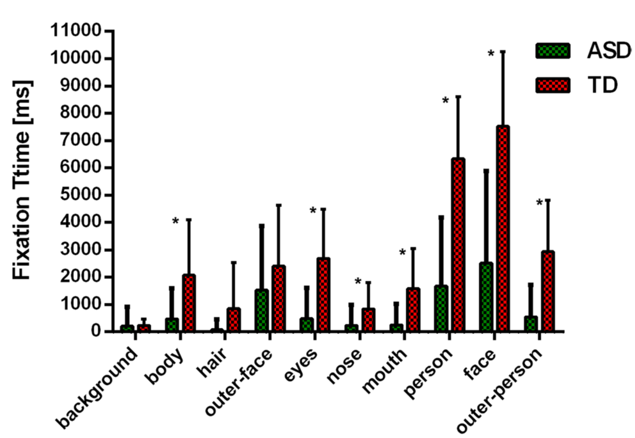

Fig. 2 Fixation times of the ten AOIs between the two groups. *$p < 0.005$ after Bonferroni correction (0.05/10)

We found that ASD children showed significantly reduced fixation time at the eyes, mouth, body, person, face, and outer-person. However, only the fixation times at the moving mouth and body could significantly discriminate ASD from TD with a classification accuracy of 85.1%, sensitivity of 86.5%, and specificity of 83.8%. Our results may shed new insights on the development of new methods for early detection and screening of ASD.

Early identification through screening and surveillance is crucial for early intervention, which may improve outcomes for children with developmental disorders such as ASD (Delahunty 2015). The American Academy of Pediatrics (AAP) recommends routine developmental screenings for specific disorders at ages 9, 18, and 30 months (or at 24 months if a 30 month visit is not planned) (Council on Children With Disabilities et al. 2006). The screening at 18 months can help identify ASD, cerebral palsy, global developmental delays, and specific language disorders. Screening for autism, global developmental delays, and specific language disorders should be repeated at the 24- or 30 month visits (Delahunty 2015).

To date, investigators have developed different screening tools, such as Checklist for Autism in Toddlers (CHAT), Modified Checklist for Autism in Toddlers (M-CHAT), Communication and Symbolic Behavior Scales Developmental Profile Infant/Toddler Checklist, Social Communication Questionnaire (SCQ), and Social Responsiveness Scale (SRS) (Lai et al. 2014). Nevertheless, current consensus is poor regarding what constitutes sufficient evidence to recommend universal or secondary screening for ASD as part of standard practice (Hampton and Strand 2015; Zwaigenbaum and Penner 2018). Studies have suggested that socioeconomic status (SES) (Scarpa et al. 2013), developmental delay (Wiggins et al. 2007), and child characteristics and family demographic factors (Moody et al. 2017) may all influence the application of these screening tools.

Recently, ASD biomarkers research has grown exponentially, and the integration of such technology into the future assessment of ASD risk is almost certain (Zwaigenbaum and Penner 2018). Nevertheless, it worth noting that current ASD biomarkers, including eye tracking, are supplementary. That is, they are not meant to serve as replacements of other clinical assessments and services.

ET may provide a unique window into the moment-by-moment selection of information for attention, and it therefore may reflect cognitive processing (Frazier et al. 2017). In this study, we presented a speaking face and investigated the gaze of 4–6-year-old children with and without ASD. We found that ASD is associated with decreased fixation time at the eyes, mouth, nose, body, person, face and outer-person compared with TD. This endorses the important role of fixation at the eyes in ET detection of autism.

Our results are in line with a previous study in which investigators applied ET to examine the gaze patterns of 6-month-old infants at high risk and low risk for developing ASD. This study presented faces that were: (1) still; (2) moving and expressing positive affect; or (3) speaking. Researchers found that infants who later developed ASD (clinically evaluated at 3 years of age) spent less time looking at the presented scenes in general compared to other infants. However, their fixation time on the inner features of the faces decreased compared with the other groups only when the presented face was speaking (Shic et al. 2014). Our results are also consistent with a recent meta-analysis of 122 independent studies with 1155 comparisons, in which the authors found that individuals with autism showed less attention to the eyes and whole-face regions, which are crucial for accurate social perception (Frazier et al. 2017).

Our results differ from a previous study that used an ET paradigm to measure the fixation time of 26 male adolescents and adults with ASD and TD (15–41 years old) using a still image, eye blinking video (an actress repeatedly opens and closes her eyes for 7 s), mouth-moving video (an actress repeatedly opens and closes her mouth for 4 s), silent face video (an actress with a still face for 3 s), and talking video (7 s) (Fujioka et al. 2016). The authors found no significant group difference in fixation time during the mouth-moving and talking stimuli, which were similar to the stimuli applied in our study. We speculate this may be due to the different ages of participants. Our results, together with the infant study (Shic et al. 2014), suggest that the mouth-moving paradigm may be more sensitive to an infant or child population.

In this study, we applied SVM to distinguish ASD from TD using fixation times of all pre-defined AOIs and ratios. SVM, a widely-used machine learning method, is a supervised learning model with associated learning algorithms that analyze data used for classification analysis. Using a set of training examples with each marked as one or the other of two categories, an SVM training algorithm builds a model that assigns new examples to one category or the other, making it a non-probabilistic binary classifier.

In a previous study, Liu et al. (Liu et al. 2016) proposed a machine learning framework to identify children with ASD based on face-scanning eye movement patterns. Eye-tracking data was obtained from a facial recognition task completed by ASD and TD children from 4–11 years old. When researchers divided the face into 64 areas, they found that the areas below the right eye, around the inner side of the left eye, and above the left lip were the most discriminative regions between ASD and TD children, with accuracy of 88.51%, specificity of 86.21%, and sensitivity of 93.10%.

In another study on male adolescents and adults with ASD, Fujioka and colleagues (Fujioka et al. 2016) applied a complex paradigm: the percent of eye fixation time allocated to particular objects depicted in videos. Such objects could include eyes and mouths in human face videos, upright and inverted biological motion in videos that presented these stimuli simultaneously, and people and geometry in videos that presented these stimuli simultaneously. Researchers found that fixation times on certain stimuli that exhibited large effect sizes for group differences could differentiate ASD from TD with a sensitivity of 81.0% and a specificity of 80.0%.

In this study, we used a short and simplified paradigm and found that only fixation time at the moving mouth and body could significantly discriminate ASD from TD with a classification accuracy of 82.8%, sensitivity of 79.3%, and specificity of 86.2%. This accuracy rate is comparable with previous studies using a much more complicated ET paradigm.

There are several limitations to this study. First, due to the limited access to the ADI-R and ADOS in China, the ASD diagnoses were made by licensed pediatric psychiatrists based on the DSM and CARS score but were not confirmed with additional validated diagnostic tools (ADOS/ADIR). Second, some indication of functional level, such as IQ and adaptive behavior, was not identified. Third, the sample size is relatively small, so future studies with larger sample sizes are needed to further validate our findings. Fourth, we do not know if the findings are specific to this particular age group. Studies on other populations, particularly young infants, are needed. Fifth and finally, a direct comparison between our paradigm and other popular paradigms, as well as combining the current paradigm with other paradigms, is also needed.

In this preliminary study, we found that fixation times at the mouth and body can significantly distinguish ASD from TD in 4–6 year-old children using a 10 s muted video clip of a female speaking. These findings may shed light on the development of new screening methods for the early detection of ASD.

Author Contributions GW, XK, YL, JK contributes experimental design; GW, BS, YL, ZW, ZF contributes data collection; SY, YT, BS, MK contributes data analysis; JK, SY, GW, XK, YT, JP, CL contributes manuscript preparation.

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Compliance with Ethical Standards

Conflict of interest JK has a disclosure to report (holding equity in a startup company (MNT) and pending patents to develop new neuromodulation tools) but declares no conflict of interest. All other authors declare no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the Shenzhen Maternity & Child Healthcare Hospital research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from parents of all individual participants included in the study. We are grateful to Georgia J Wilson for her help in revising the manuscript.

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