Impaired exploratory eye movements in children with Asperger's syndrome.

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Abstract

Objective: Previous eye-tracking studies using an eye mark recorder have reported that disturbances in exploratory eye movements in adult schizophrenic patients are associated with social functioning. The current study sought to determine whether exploratory eye-movement disturbances are present in children with Asperger's syndrome (AS) compared with typically developing (TD) children.

Materials/Participants: The participants were 23 children with AS and 23 age-matched TD children. We measured exploratory eye movements using an EMR-8B eye mark recorder and an exploratory eye movement-measuring device.

Method: Eye movements were recorded while participants freely observed a geometric figure (free viewing task), and while they complied with the instructions of an experimenter (repeat-comparison task). We assessed eye fixation points (EFPs) and total eye scanning length (TESL) in all tasks, and measured the responsive search score (RSS) in the repeat-comparison task.

Results: In the free viewing task, children with AS exhibited significantly shorter TESL compared with TD children. In the repeat-comparison task, children with AS exhibited significantly lower RSS. Autism Spectrum Screening Questionnaire scores were

negatively correlated with both EFP and TESL, but not RSS.

Conclusion: The current results revealed that children with AS exhibited dysfunction in exploratory eye movements. Thus, assessing exploratory eye movements in a repeat-comparison task may be useful for detecting social impairment among children with AS.

Keywords: Asperger's syndrome; Eye-tracking technology; Exploratory eye movements; Responsive search score; Social interactions

1. Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by a triad of impairments: social communication problems, difficulties with reciprocal social interactions, and restricted repetitive and stereotypical patterns of behavior, interests, and activities [1]. Approaches to studying social impairment, a core feature of ASD, have become increasingly sophisticated in recent years, both in terms of methodology and in extending experimental research [2]. In the 1970s, Ornitz et al. examined parental reports of specific social behaviors rather than direct observation and characterization [3]. In the 1990's, Osterling and Dawson examined home videos of ASD individuals to assess social, affective, joint attention, and communicative behaviors and specific autistic symptoms [4]. Klin et al. (2002) investigated the ways in which cognitively able males with autism observe social situations, using infrared eye-tracking technology. The authors measured visual fixation patterns while viewing video footage of naturalistic social situations. Individuals with autism were found to exhibit abnormal patterns of social visual pursuit consistent with reduced salience of the eyes and increased salience of the mouth, the body, and other objects [5].

Kojima et al. used an eye mark recorder that uses infrared eye-tracking technology to examine eye movements (EMs) of schizophrenic and non-schizophrenic patients while the patients viewed geometric figures. The authors examined EMs in schizophrenic patients while they freely viewed geometric figures. These 'exploratory' EMs are thought to reflect voluntary attention to a greater extent than pursuit EMs [6]. In addition to this free viewing condition, the authors also examined EMs while participants explored a geometric figure after being asked a series of questions about the figure by the experimenter. The results revealed a negative correlation between exploratory eye movements and negative symptoms such as blunted affect and emotional withdrawal, as assessed by the Brief Psychiatric Rating Scale in patients with schizophrenia. As such, the authors concluded that their method can be used to assess reciprocal interactions in schizophrenic patients.

In the current study, we hypothesized that reciprocal interaction may be used to assess children with AS, by measuring exploratory eye movement with eye-tracking technology. To test this prediction, we compared EMs of children with AS with those of typically developing (TD) children, examining whether exploratory EMs are impaired

in children with AS.

2. Methods

2.1. Materials and Participants

This study involved 23 children with AS (20 males, three females), and 23 age-matched TD children (21 males, two females). Children with AS were diagnosed according to the criteria described in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [1]. All children with AS underwent clinical evaluation by a psychologist, and diagnosis was performed by four pediatric neurologists (TO, SN, YY, and TM). Among 23 Children with AS, three were medicated with risperidone, two with methylphenidate, one with atomoxetine, and one with paroxetine. TD children were recruited as paid volunteers. An experienced pediatric neurologist and an experienced psychologist obtained participants' medical history and performed neurological examination. Eligibility criteria for TD children included an absence of abnormalities in developmental, behavioral and academic history, confirmed by neurological findings. Informed consent was obtained from all participants and parents after the details of the study had been fully explained. The Ethical Committee of Kurume University School of

Medicine approved the study protocol. We measured exploratory eye movements using an EMR-8B eye mark recorder (NAC Co, Tokyo, Japan) and an exploratory eye movement-measuring device, which is patented in Japan by Kojima et al. (Patent Number: 4357200). Eye-tracking was conducted only in those participants who could maintain eye fixation during calibration.

2.2. Eye movement recording

Participants sat on a chair with their eyes positioned 425 mm from a monitor displaying the target figures. A camera detecting corneal reflection of infrared light (850 nm) was used to identify eye movements, which were analyzed automatically. Movements > 1° with duration > 0.1 sec were scored as an eye movement. Exploratory eye movements were examined by presenting an S-shaped figure, then measuring the number of eye fixation points (EFPs), the total eye scanning length (TESL) and responsive search score (RSS) following the method described by Kojima et al. [6].

2.3. Measurement protocol

For Session 1 (free-viewing task), each participant was presented with an initial S-shaped figure (Fig. 1) for 15 seconds and asked to memorize it. The S-shaped figure had two protrusions (indicated by arrows in Fig. 1). We measured the number of EFPs and the TESL while participants freely viewed the figure.

For Session 2 (repeat-comparison task), participants were presented with an S-shaped figure in which one of the protrusions was shifted (Fig. 1), and were asked if they observed any difference between this figure and the original one. After the participant responded to the question correctly, the experimenter asked whether there were any other differences. This same final question was repeated until the participant answered there was no difference. We measured responsive eye movements for 5 seconds while participants viewed the figure after the final question.

Session 3 (repeat-comparison task) was a repetition of Session 2 using an S-shaped figure without projections (Fig. 1).

2.4. Eye-movement measurements

Measurement of the number of EFPs

An EFP was defined by a fixation time exceeding 0.1 sec. Total EFP refers to the total number of EFPs in repeat-comparison tasks.

Measurement of total eye scanning length (TESL)

Eye scanning length is defined as the distance between two EFPs. TESL was measured while participants viewed the original figure for 15 seconds in Session 1, and for 5 seconds after the final question in the repeat comparison task (Sessions 2 and 3). Total TESL refers to the total length of TESL in the repeat-comparison task.

Measurement of responsive search score (RSS)

The S-shaped figures used in the repeat comparison task were each divided into seven sections (Fig. 2). RSS was estimated as the total number of sections, and EFPs were located in each section. In Sessions 2 and 3 as described above, we examined the sections in which the participants fixed their eyes once or more during the 5 seconds following the final question. Thus, there was a maximum score of 7 for each figure. Total RSS refers to the sum of scores of RSS in repeat-comparison tasks.

2.5. Clinical symptoms and intellectual level

To evaluate the clinical symptoms of children with AS, we asked each participant's caregiver and teacher to complete the Autism Spectrum Screening Questionnaire (ASSQ) [7]. The ASSQ is a 27-item checklist for completion by lay informants when assessing characteristic symptoms of AS and high-functioning autism in children and adolescents with normal intelligence or mild mental retardation. The ASSQ allows for rating on a 3-point scale (0, 1, or 2; 0 indicating normality, 1 indicating some abnormality, and 2 indicating definite abnormality). The range of possible scores was 0-54. Cutoff scores of 19 for parent ratings and 22 for teacher ratings have been previously suggested as reasonable trade-off scores for identifying ASD [7]. The level of intellectual functioning was measured using the Wechsler Intelligence Scale for Children-Third Edition (WISC-III). Each of these scores and subscales was compared with eye-movement components.

2.6 Statistical analyses

We compared eye movement parameters between children with AS and TD children using the Mann-Whitney U test. In addition, we compared these parameters

between male and female TD children. Correlations between age and the basic components of exploratory eye movements in groups of children, and between the elementary components of exploratory eye movements and AS symptoms were expressed as Pearson product-moment correlation coefficients (r). Values are presented as mean ± standard deviation (SD).

3. Results

We analyzed data from 52 participants, excluding six participants who were unable to maintain fixation during calibration. The mean age of children with AS (n = 23) was 12.1 (2.6), and the mean age of TD children (n = 23) was 11.4 (1.6); no significant difference was found ($t = 1.087$, $p = 0.283$). The mean ASSQ scores, as evaluated by caregivers and teachers, were 21.0 (9.1) and 23.5 (8.0), respectively. Mean scores for Full IQ, Verbal IQ, and Performance IQ in children with AS were 100.7 (14.6), 101.2 (14.7), and 100.0 (15.5), respectively. Fig. 1 shows typical EFP values for both a child with AS and a TD child.

3.1. Eye fixation points (EFP)

In all sessions, there were no significant differences between EFPs among children with AS and TD children (Table 1).

3.2. Total Eye Scanning Length (TESL)

In Session 1, children with AS exhibited significantly shorter TESL than TD children ($p = .027$). In Sessions 2 and 3, and total TESL, children with AS exhibited slightly shorter TESL values, but there were no significant differences (Table 1).

3.3. Responsive Search Score (RSS)

Children with AS exhibited significantly lower RSS than TD children in Sessions 2 and 3 ($p = .009$ and $p = .001$, respectively; Table 1), as well as total RSS ($p = .001$; Table 1).

3.4. Correlation between clinical symptoms and elementary components of exploratory eye movements in children with AS.

We found a significant negative correlation between EFPs in Session 3 and ASSQ scores, as rated by caregivers and teachers ($r = -0.460$; $p = 0.027$ and $r = -0.469$; $p = 0.024$, respectively), and between total EFP and ASSQ scores rated by caregivers (r

= -0.595; p = 0.003) (Fig. 3). The results also revealed a significant negative correlation between total TESL and ASSQ scores rated by caregivers (r = -0.432; p = 0.040). No significant correlation was identified between total TESL and ASSQ scores rated by teachers (r = -0356; p = 0.096) (Fig. 3). Likewise, no significant correlation was found between RSS values (in Sessions 2 and 3, and total RSS) and ASSQ scores (data not shown). In addition, we found no significant correlations between the elementary components of exploratory eye movements and any WISC-III scores or subscales, or any significant differences between males and females (data not shown).

4. Discussion

In the current study, EFP and TESL were measured during a free viewing task. The results revealed that, compared with TD children, children with AS exhibited significantly shorter TESL, and no significant EFP. Short TESL without significant EFP indicates that the speed of eye movement among AS children was slower than that of TD children. A number of previous studies have reported dysfunction in aspects of oculomotor function among cognitively able patients with ASD, including saccadic eye

movements [8] and pursuit eye movements [9]. The current results might be related to previous findings of oculomotor dysfunction in ASD. However, we observed no significant EFP or TESL in Sessions 2 and 3. The novel results in these sessions suggest that differences in psychological factors such as exploration of differences in the figure, as well as oculomotor abnormalities, may have influenced the results.

In the repeat-comparison task, we measured EFP, TESL and RSS, which occurred in response to the experimenter asking for the last time whether the participant observed any further differences. This verbal interaction between the participant and experimenter is a unique aspect of the current study. Following the experimenter's question, TD children explored the figure again, examining the other sections of the figure. This further exploration was reflected by higher RSS scores, even though participants detected no differences following the final question. Children with AS exhibited significantly reduced RSS compared with TD children, but no significant differences were found between groups in TESL or EFP. This result suggests that children with AS tended to repeatedly view only limited sections of the figure. RSS

reflects visual behavioral responses, measured while participants checked or confirmed the figure as a part of a social interaction between the participant and the experimenter. Therefore, RSS may also provide an indicator of the effects of AS on interpersonal response, as reported in schizophrenic patients [6]. In addition, the results of our repeat-comparison task revealed negative correlations between ASSQ scores and the parameters of exploratory eye movements, including EFP and TESL, in children with AS. Such correlations were found only repeat comparison task, revealing that low RSS with fewer EFPs and shorter TESL in the repeat comparison task were associated with more severe autism symptoms. A previous eye-tracking study assessing social dysfunction in ASD measured visual fixation patterns while participants viewed videos depicting naturalistic social situations [5]. In this previous study, the best predictor of autism was reduced eye region fixation time, and the amount of fixation on mouths and objects was significantly correlated with social functioning. Although the current study used inanimate figures for testing, our method is still able to examine certain aspects of social dysfunction in ASD. The portability of the exploratory eye movement recording apparatus means it can be conducted in various locations, including outpatient clinics,

and a skilled experimenter is able to complete the non-invasive measurement in 4-5 minutes.

The low RSS with normal TESL exhibited by children with AS suggests that they tended to repeatedly view the same sections of the figure compared with TD children. Shah and Frith reported that patients with ASD have a tendency to attend to local as opposed to global features, proposing that this phenomenon is caused by weak central coherence as a characteristic of information processing in ASD [10]. The authors assessed the characteristics of information processing in ASD using a Wechsler block design task, suggesting that autistic participants require less effort to segment a gestalt. In addition, other studies using visual cognitive tasks have reported that ASD individuals exhibit a high level of attention to detail [11-13]. The present finding that AS individuals viewed the same sections repeatedly without searching for other possible differences may reflect a characteristic feature of information processing in ASD.

Previous studies by Kojima et al. using the same methodology revealed that a group of adults with chronic schizophrenia exhibited lower RSS than a normal control

group and an obsessive-compulsive disorder group [11-13], indicating that low RSS may be a specific feature of schizophrenia. In the current study, RSS was also found to be significantly reduced among children with AS. Although early reports by Kanner concluded that autism and schizophrenia are unrelated [14], and several studies in the 1970s [15, 16] confirmed that autism is reliably distinct from schizophrenia, these disorders involve some similar symptoms [17]. While the current findings indicate that RSS is not specific to patients with schizophrenia, the low TESL reported in patients with schizophrenia [18] was not observed in children with AS in the present study.

A recent study using functional magnetic resonance imaging during a complex social cognition task reported that individuals with ASD and schizophrenia exhibited significantly reduced neural activation in brain regions involved in processing social stimuli, including the amygdala, fusiform face area, and ventrolateral prefrontal cortex, compared with healthy controls [19]. These results suggest that the same pattern of abnormal neural mechanisms may underlie the specific social cognitive deficits exhibited in AS and schizophrenia.

The present study has several limitations. First, we evaluated autistic

symptoms using the ASSQ, which assessed not only reciprocal social interactions but also social communication problems and restricted repetitive and stereotypical patterns of behavior, interests, and activities. In Japan, there is no standardized questionnaire that assesses only dysfunction of reciprocal social interactions or social competence. Thus, we cannot conclude that our results relate only to dysfunction of reciprocal social interactions. Second, RSS was not significantly correlated with ASSQ score. Although low RSS was a characteristic feature in patients with AS, it did not correlate with the severity of symptoms. Based on these findings, we propose that RSS should be assessed together with TESL and EFP. Third, we did not examine WISC-III or ASSQ in TD children. All TD children studied in ordinary classrooms, and participants with AS or any other psychiatric disorders were identified through brief interviews with caregivers/children and behavioral observation, and excluded from the TD group.

In conclusion, measuring exploratory eye movements with a repeat-comparison task revealed a difference between children with AS and TD children, and this difference was correlated with clinical symptoms. These findings suggest that exploratory eye movements can be used to examine social dysfunction among children

with AS.

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Conflict of interest

None of the authors has any conflict of interest to disclose.

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Figure Legends

Figure 1. The upper row shows the S-shaped figures. Left: an initial S-shaped figure with two protrusions. Middle; an S-shaped figure in which one of the protrusions has shifted. Right: an S-shaped figure without protrusions. The second and third rows show a typical series of eye movements in the participants of each group. Small circles indicate EFPs.

Figure 2. Scoring of responsive search score (RSS). The figure is divided into seven sections. The number of the sections on which the subject actually focused (shown by the white circle and line) shows the responsive search score (RSS). In this case, the RSS was seven. Small circles indicate EFPs.

Figure 3. The correlation between ASSQ score and the parameters of exploratory eye movements in Asperger's syndrome: Left; ASSQ score evaluated by caregivers. Right;

ASSQ scores evaluated by teachers. The upper row shows the EFP in Session 3 and ASSQ scores, the second row shows the total EFP and ASSQ scores, and the third row shows the total TESL in Session 3 and ASSQ scores. We found a significant negative correlation between EFPs in Session 3 and ASSQ scores evaluated by caregivers, and by teachers ($r = -.460$; $P = .027$ and $r = -.469$; $P = .024$, respectively); between total EFP and ASSQ scores evaluated by caregivers ($r = -595$; $P = .003$); and between total TESL and ASSQ scores evaluated by caregivers ($r = -.432$; $P = .040$).

Fig. 1

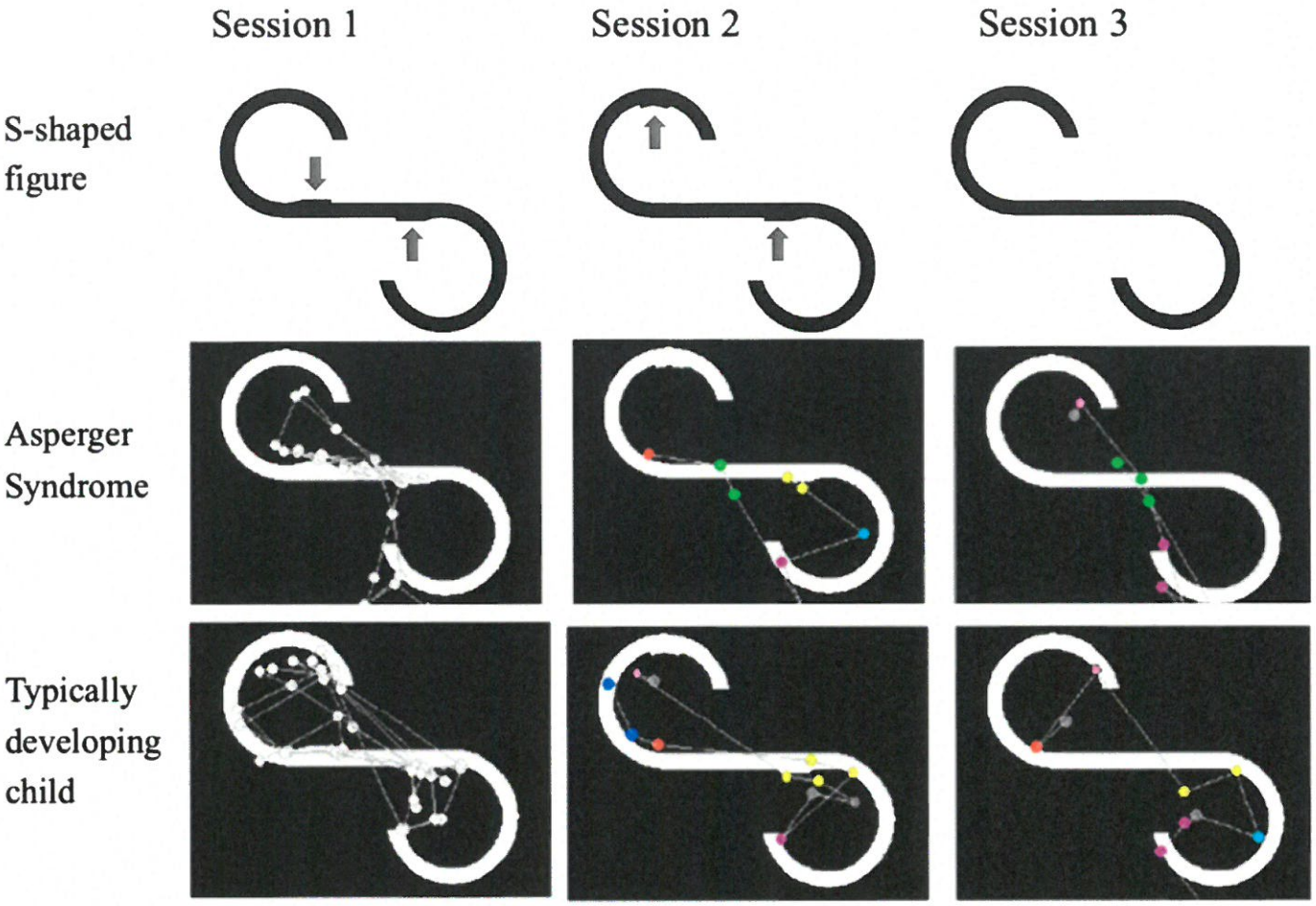
Session 1
Session 2
Session 3
S-shaped figure
Asperger Syndrome
Typically developing child

Fig. 2

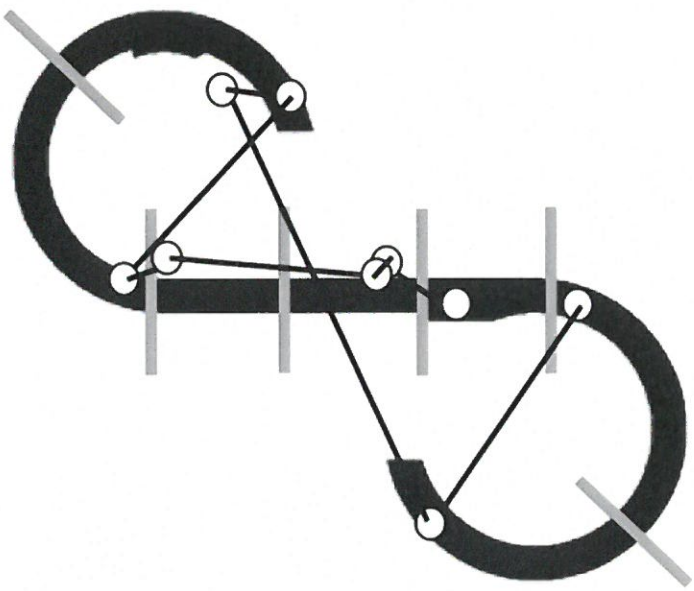

Fig. 3

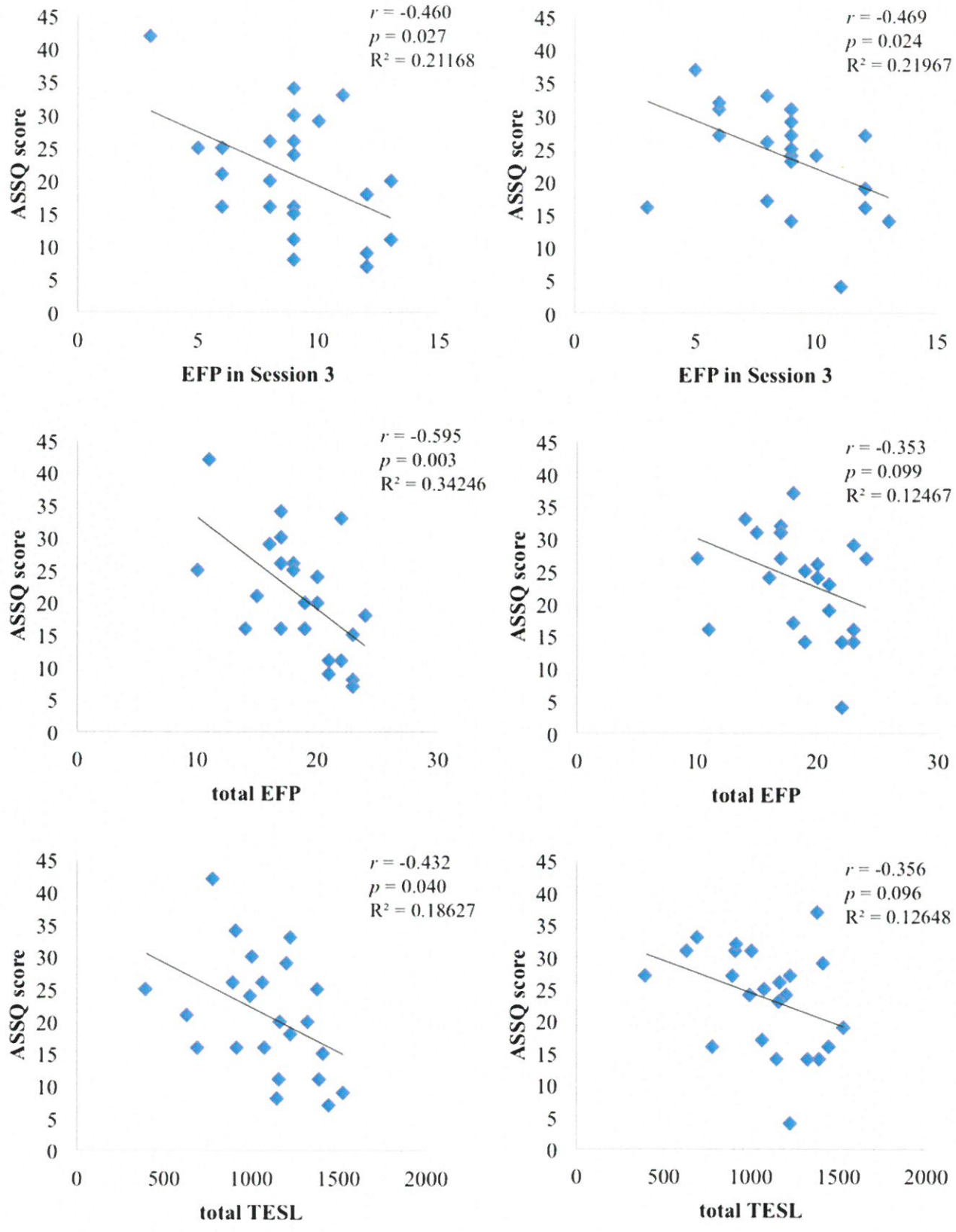
r = -0.460
p = 0.027
R² = 0.21168
ASSQ score
EFP in Session 3
r = -0.469
p = 0.024
R² = 0.21967
ASSQ score
EFP in Session 3
r = -0.595
p = 0.003
R² = 0.34246
ASSQ score
total EFP
r = -0.353
p = 0.099
R² = 0.12467
ASSQ score
total EFP
r = -0.432
p = 0.040
R² = 0.18627
ASSQ score
total TESL
r = -0.356
p = 0.096
R² = 0.12648
ASSQ score
total TESL
Caregiver
Teacher

Table 1 The components of exploratory eye movements compared between children with Asperger's syndrome and typically developing children

			Session 1		Session 2			Session 3					
	n	age	EFP	TESL	EFP	TESL	RSS	EFP	TESL	RSS	total EFP	total TESL	total RSS
AS	23	12.1	28.2	1330*	9.7	551	3.1*	8.9	533	3.2*	18.6	1084	6.3*
		(2.6)	(4.9)	(405)	(2.7)	(200)	(1.2)	(2.6)	(215)	(1.2)	(3.8)	(284)	(1.9)
TD children	23	11.4	31.6	1698	10.1	563	4.1	10.2	640	4.5	20.3	1203	8.5
		(1.6)	(6.3)	(536)	(3.3)	(209)	(1.2)	(3.2)	(291)	(1.1)	(5.7)	(433)	(1.9)

Values are expressed as mean ± standard deviation (SD)

AS, Asperger syndrome; TD, typically developed children; EFP, eye fixation points; TESL, total eye scanning length; RSS: responsive search score * Indicates significant difference from TD children ($p < 0.05$).