Applications of Eye Tracking in the Diagnosis of Early Stages of Autism Spectrum Disorders

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Abstract: In this project we designed a computerized diagnostic test procedure to measure gaze parameters known to be related to early symptoms of Autism Spectrum Disorders (ASD) (saccades and smooth pursuit eye movements). An eye-tracker was used to gather gaze data. Custom visual stimuli and guidelines for collecting eye tracking data from the subject group (children between 12-24 months of age) were developed. A first proof of principle study was performed on three children without suspected clinical diagnosis in the target age range. The results were promising and the procedure seems to be applicable to small children. Further work needs to be carried out in order to validate whether the procedure actually will be a good diagnostic support tool in clinical settings.

1 INTRODUCTION

The aim of the research is to understand how eye tracking technology can be used for the early detection of Autism Spectrum Disorders (ASD) in children younger than the average age for diagnosis. ASD is a complex neurodevelopmental disorder which affects behavior, communication and social functioning (APA, 2017). It can be diagnosed as early as 15 - 18 months of age. Even so, the average age of diagnosis is about 4.5 years, and some subjects are not diagnosed until adulthood (APA, 2017).

As Bölte et al. (2016) describe, research into early stages of ASD make use of various methods for examining the children development and responses to interventions, right from the first months and years of life. The methods can be classified into two groups: (1) informant and clinician-based behavioral methods (e.g. questionnaires, observation scales, interviews and developmental tests), which are more based on observation, subjective and sometimes qualitative; (2) technology based and/or measurements of basic cognitive or neurological processes and structures (e.g. eye tracking, electroencephalography (EEG), functional and structural magnetic resonance imaging (MRI)), which are more direct, objective and mostly quantitative. It is conceivable that eye tracking can be used as an integrated part of screening and diagnostic assessments in the future (Falck-Ytter et al., 2013).

Diagnosing ASD in the first 24-30 months of life of a child poses particular challenges to clinicians, among which that there are no objective diagnostic biomarkers for ASD (Samad et al., 2017). Issues in sensorimotor control are involved in ASD (Johnson et al., 2016), therefore tools for measuring these kind of deficits are promising. A particularly promising application of eye trackers is the study on young children, in order to capture early-emerging developmental mechanisms in this critical period of the development and to illuminate the early course and characteristics of ASD. Indeed, eye tracking has already been largely used in studies on people with ASD (for some recent reviews, see Bölte et al., 2016; Falck-Ytter et al., 2013; Frazier et al., 2017; Johnson et al., 2016; Papagiannopoulou et al., 2014).

Eye trackers can provide measurements on eye movements which are impossible to assess with naked eye (e.g. saccades, smooth pursuit). Remote eye trackers (infrared / corneal reflection types) are unobtrusive and do not constrain movements, which makes them ideal to use on small children for early diagnosis (Bölte et al., 2016; Falck-Ytter et al., 2013; Samad et al., 2017).

The present on-going study does not aim to develop an eye tracking procedure with inherent diagnostic value, but it aims to develop a framework (consisting of a rationale of relevant eye parameters and the methods to measure them) and a procedure which proves to be applicable to the target children. The study intends to apply the findings in the eye tracking

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scientific literature to clinical settings for ASD diagnosis. We started the research work as a Master Thesis (Dalai, 2018) and we intend to refine and improve the tentative procedure outlined in this paper by doing further research, until in the future we will be able to assess its clinical diagnostic value.

In this context, we see the eye tracking technologies as a supporting tool for ASD diagnosis, which are designed to be used together with the already validated behavioral diagnostic praxis. Given the complexity of ASD, it is fundamental to have a rich description of the children's development condition, including quantitative and qualitative measurements. The current screening and diagnostic tests (see Magán-Maganto et al., 2017; Towle and Patrick, 2016; Charman and Gotham, 2013) already assess qualitatively atypical gaze behaviors as a sign of ASD. Even so, the clinicians need to assess many other complex behavioral manifestations related to ASD in order to formulate a diagnosis. Eye tracking alone cannot provide a definitive answer, but it can provide useful evidences to support clinical decision making.

2 BACKGROUND

We reviewed literature with the aim of identifying those eye-tracking metrics which seem to be suitable to support early ASD diagnosis. The vast majority of the collected literature shows results from experiments done on adolescents and/or adults with ASD (see for example the review by Johnson et al. (2016)), while the number of studies involving small children in the early diagnosis age range is rather low (see for example the review by Falck-Ytter et al. (2013)). Even the few studies which have found differences in specific eye parameters between typically developing and ASD groups, have been carried out on subjects in older age groups. This offers one of the motivations to start a systematic experimentation with the target children group.

So far, the eye parameters we have identified in literature as potential useful early ASD markers are: standard deviation of saccade gain (Johnson et al., 2016), open-loop and closed-loop smooth pursuit gain (Johnson et al., 2016; Takarae et al., 2004). Up to this point, we have left aside the analysis on fixations on Areas of Interest (AOI), due to the difficulty in determining the ecological validity of the stimuli in a controlled experimental setting. We left aside also the analysis on pupil diameter, since this parameter is sensitive to environmental lightning and it is difficult to assess consistently in a variety of different clinical settings. The framework focuses on the assessment of saccades and smooth pursuit eye movements, which require high frequency and precision measurements and also a more controlled experimental environment. These two condition suit better eye tracking technology.

Discussing with a speech therapist expert in ASD diagnosis (Minichiello, S., 2017, personal communication) it emerged that a possible validation process for the usage of eye trackers in this clinical context requires the following steps: (1) defining the steps of age for testing with the children (e.g. 18-24-36 months of age); (2) recording a series of eye tracking measurements on a typically developing group, in order to collect baseline data and to assess the reliability of the measurements; (3) administering the same procedure on ASD children, in order to assess differences between groups.

3 METHODS

Conducting eye tracking studies on small children poses a series of challenges. Small children cannot be instructed to behave in a certain way or to focus on a stimulus for a certain period of time, due to their obvious lack of linguistic competence for understanding complex task instructions. Therefore, the visual stimuli need to be salient and interesting enough to be followed with the gaze by the children, without further prompting by the researchers. Another issue is to keep the children's interest over the whole experiment time. Short trials displaying simple eye-catching visual stimuli should be staggered with some audiovisual contents as interstimulus materials, in order to keep the children entertained and provide variety and playfulness.

3.1 Apparatus

We carried out a first iteration of testings, as a proof of principle, by using a SMI® RED250mobile™ eye tracker. Its sample rate is up to 250 Hz, which is sufficient for tracking saccades, smooth pursuit movements and fixations with great accuracy. It is mounted on a laptop computer, underneath a 15.6 inch display monitor (refresh rate 60 FPS, covering around 39 degrees of visual angle horizontally and 22 degrees vertically at 50 cm of distance, resolution 1920x1080 px). The setup is portable and can be carried around and used in different settings.

3.2 Setting

The research protocol follows the guidelines provided by Sasson and Elison (2012) for eye tracking studies on young children with ASD. The light in the room should be kept a bit dim, in order to encourage the child to focus on the display monitor on which the visual stimuli are presented. The caregiver sits on a chair (positioned in front of the screen at an adequate distance) and the child sits on the caregiver's lap throughout all the experiment, in order to make both the child and the parent feel more at ease. Depending on the location, the researchers can use an external monitor connected to the eye tracker laptop computer, and they operate the computer in a position out of the child's sight. If the use of an external monitor is not practical or not feasible (as it was in the first proof of principle study), the researchers start the eye tracking experimental routine on the laptop and let it run until the end, placing themselves far away enough to not disturb the experiment.

3.3 Procedure

The experiment consist of four different phases:

- Introduction and setup phase: The caregiver and the child take a seat, and they are administered the informed consent form. In the meantime, a video is shown on display monitor, in order to start to capture the child's attention;
- Calibration phase: When the caregiver feels that he/she and his/her child are comfortable and ready to start, a calibration routine is shown on the display monitor;
- Visualization phase: A series of videos is shown on the screen. Some of the them are stimuli materials, others are inter-stimulus materials with the aim of keeping the child entertained, but which are not suitable for eye tracking measurements;
- Conclusion phase: When the series of stimuli is over, a message is displayed on the display monitor and the test is ended.

The detailed experimental protocol has been sent for approval to the Norwegian Regional Committees for Medical and Health Research Ethics (REK), which did not raise any issue concerning the procedure.

3.4 Stimuli

We identified appropriate experimental paradigms for each eye parameter of interest, leading so far to the development of four kinds of stimuli which we put together in a single experimental procedure:

- Sinusoidal motion stimuli, assessing closed-loop smooth pursuit gain (von Hofsten and Rosander, 1997);
- Triangular motion stimuli, assessing closed-loop smooth pursuit gain (von Hofsten and Rosander, 1997);
- Step ramp task, assessing open-loop and closed-loop smooth pursuit gain (Takarae et al., 2004);
- Step paradigm (Zalla et al., 2016) for visually guided saccade tasks, assessing the standard deviation of saccade gain (Johnson et al., 2016).

We followed the recommendations from Smyrnis (2008) in order to set up the parameters for the creation and the presentation of the stimuli, among which sampling frequency ($\geq$200 Hz), amplitude ranges, direction of movement, number of cycles, etc.

In order to attract the children's attention only on the moving target in the stimuli, we designed it as the only colored element in the scene, while the background was medium-gray.

We generated the visual stimuli programmatically by developing scripts in the Processing 3 software, which is based on the Java programming language. The executive files are parametric and they allow the researchers to manipulate the stimuli variables. The software generates the visual stimuli automatically, taking care for example of the conversions between measurement units (pixels to degrees of visual angle), the drawing of periodic waves starting from trigonometric parameters, the rendering of the target movement, etc. Due to the fact that the stimuli are parametric, they can be adapted to be used on different devices and for different experimental designs. Figures 1, 2, 3 and 4 illustrate schemes and visuals from the experiment stimuli.

4 EXPECTED RESULTS

The experimentation has not fully started yet, but we have started the recruitment process. We carried out a first small proof of principle study (Dalai, 2018, pp. 53–81) on three typically developing children (9, 15 and 24 months of age, all female) in order to assess the applicability of the procedure to target subjects and the effectiveness of the eye tracking technology to collect the eye parameters of interest. We analyzed qualitatively the eye tracking records of the experiment subjects and compared the records with the ones of on an adult subject (male, 25 years old) with no vision deficiencies an no clinical diagnosis. The adult subject's records acted as reference dataset. As an example of the kind of data we collected, Figure 5

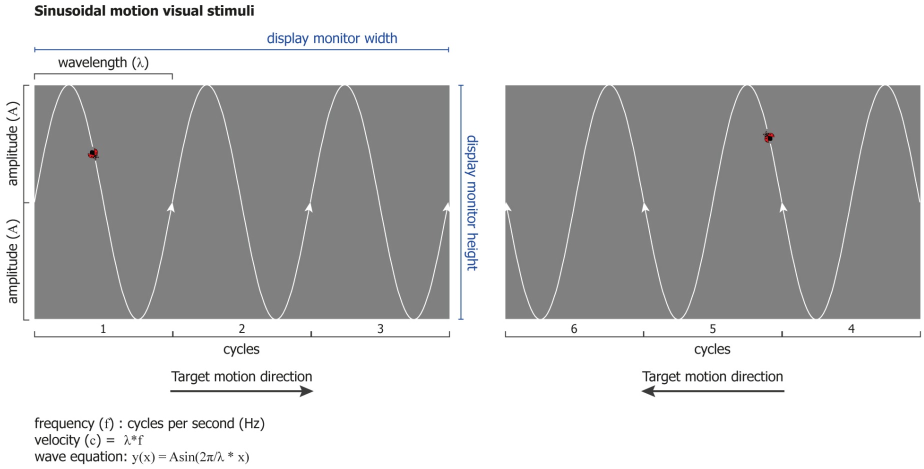

Figure 1: Scheme of the sinusoidal motion stimuli. Reworking from Dalai (2018, p. 59).

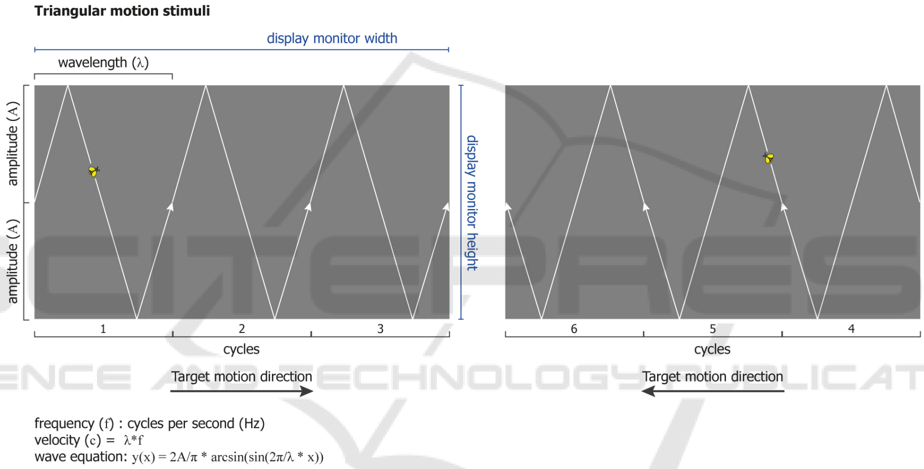

Figure 2: Scheme of the triangular motion stimuli. Reworking from Dalai (2018, p. 59).

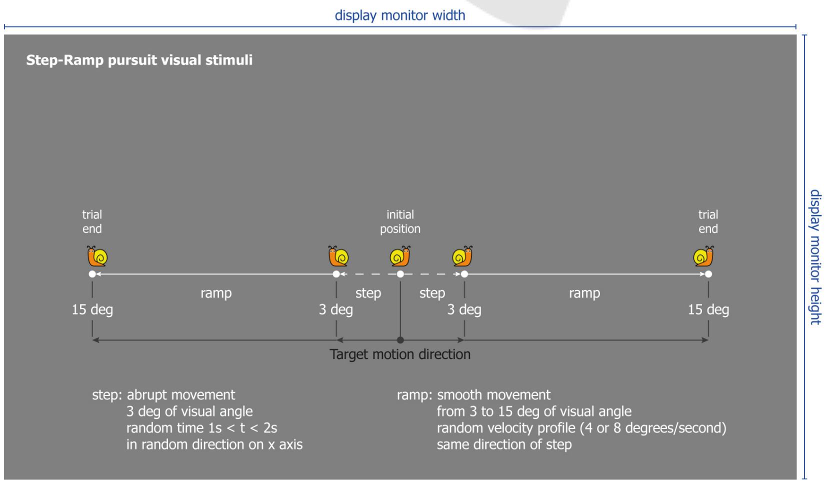

Figure 3: Scheme of the Step-Ramp stimuli. Reworking from Dalai (2018, p. 60).

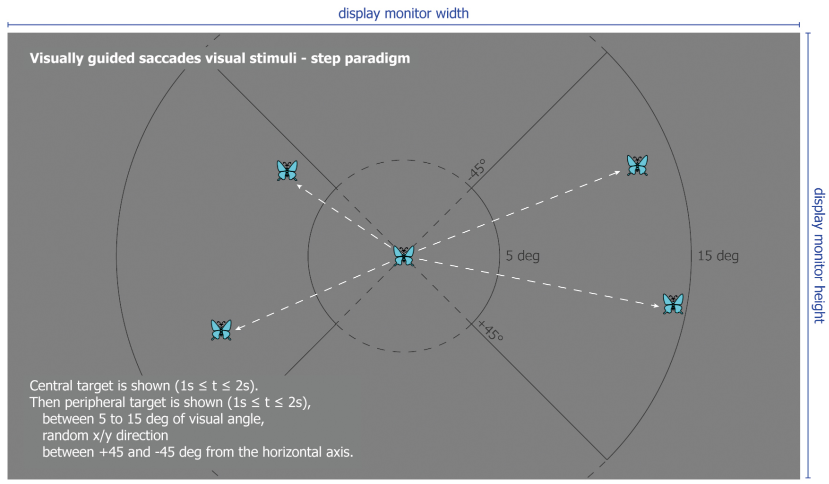

Figure 4: Scheme of the visually guided saccades stimuli. Reworking from Dalai (2018, p. 61).

shows the eye tracking record of the adult subject, and Figure 6 shows the record of the 24 months old subject. All the graphs have been outputted by the SMI eye tracker software. In the graphs it is possible to observe similar gaze patterns.

The framework and procedure seem to elicit the expected gaze patterns in the children, while improvements are needed in terms of timings, quantity of recorded data, some stimuli parameters (e.g. target velocity) and guidelines for the setting. Indeed, even if the procedure elicits the right quality of gaze patterns, the quantity of recorded data is still low overall. Table 1 shows some metrics of the proof of principle study with the target group. The tracking ratio is a quantitative metric outputted by the eye tracker software, which describes how much eye movement data was collected during a trial, and basically how efficient was the eye tracker in collecting data. The researchers determined the percentage of correctly performed repetitions by analyzing visually the graphs outputted by the eye tracker software. A high percentage of correct repetitions of the same gaze pattern strengthens the reliability of the measurements. It is more of a qualitative metric: the lower it is, the more the correct gaze patterns are scattered and not continuous. A low percentage might be due to the children's lack of attention to the stimuli target, or to the children moving too far away from the eye tracker or in other directions. The last metric was determined qualitatively by the researchers, stating if overall it was possible to detect in the graphs the expected gaze patterns under investigation. The children's records show the expected gaze patterns for the custom visual stimuli in 9 out of 10 total performed trials. Therefore, the procedure shows potential to analyze specific types of eye movements in the target children, if not younger subjects.

We analyzed the eye tracker records with the aim to highlight possible improvements for the procedure and no judgement was done on the children's performance. More refined and sophisticated algorithms for the analysis of the data are needed in order to discern clearly between the various types of eye movements and analyze them statistically (see for example (Giordano et al., 2017; Jansson and Medvedev, 2013; Larsson et al., 2015)). Nevertheless, we have already developed preliminary guidelines for the computation of the parameters of interest from the eye tracking records and we have identified improvements for the experimental procedure and stimuli. In particular, the experimental design needs to balance better the duration of the presentation of the stimuli with the necessary amount of stimuli repetitions needed for recording a reliable amount of data. The active collaboration of the caregivers helps in redirecting the attention of the children towards the display monitor.

The study will contribute to formulate a clearer hypothesis for a future validation study of the procedure, which will aim to support clinical diagnostic decisions. Systematic measurements conducted on target children and in collaboration with clinical personnel will provide the necessary data about the eye parameters of interest. The data will allow to assess the validity of oculomotor performance as an early ASD indicator. Collaborations with mathematicians and software engineers will allow to complete the framework in its data analysis part. An on-going dialogue with cognitive- and neuro-scientists will also allow to investigate further on which neural pathways could be involved in the divergent development of the oculomotor control in ASD.

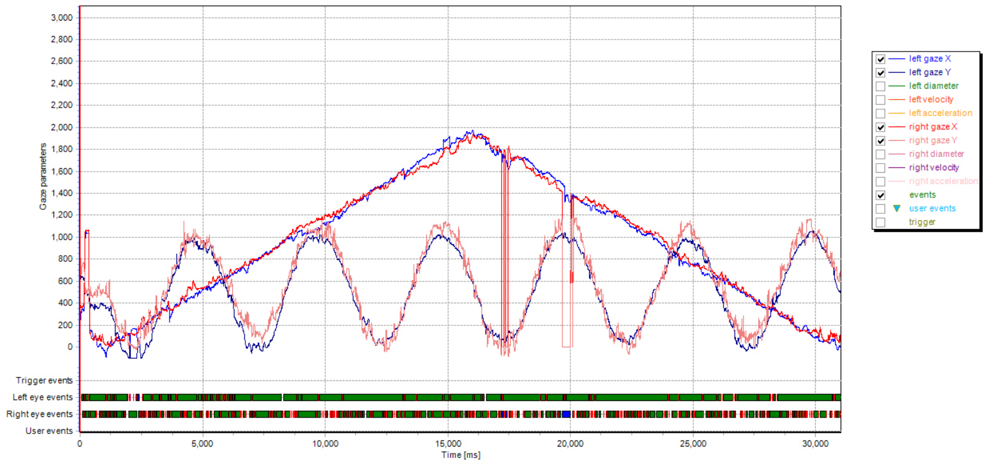

Figure 5: Pilot test eye tracker record, 25 years old, male, no clinical diagnosis, sinusoidal motion target. Picture taken from Dalai (2018, p. 66).

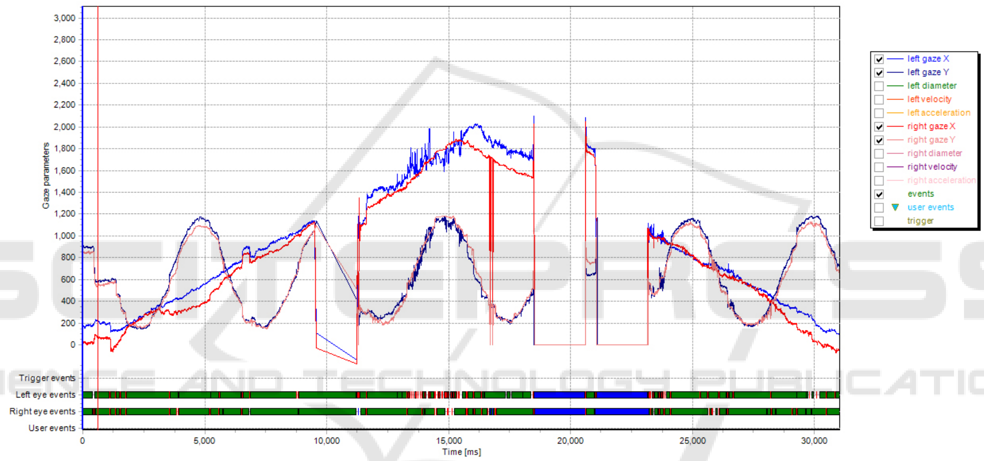

Figure 6: Participant's eye tracker record, 24 months old, female, no clinical diagnosis, sinusoidal motion target. Picture taken from Dalai (2018, p. 72).

Table 1: Summary of the experiment preliminary results. Reworking from Dalai (2018, p. 70).

Participant (Age months)	Test	Trial n.	Stimulus	Tracking ratio (%)	Repetitions (%)	Correct pattern
P1 (15)	1	1	Sinusoidal	58,8%	≈50% (3/6)	Yes
		2	Triangular	71,6%	≈33.$\bar{3}$% (2/6)	Yes
		3	Step-Ramp	79,3%	≈75% (6/8)	Yes
		4	Saccades	37,9%	≈20% (3/15)	Yes
P2 (24)	2	1	Sinusoidal	78,7%	≈75% (4.5/6)	Yes
		2	Triangular	54,9%	≈33.$\bar{3}$% (2/6)	Yes
		3	Step-Ramp	10,7%	0% (0/8)	No
		4	Saccades	Not performed	–	–
P3 (9)	3	1	Sinusoidal	23,6%	≈16.$\bar{6}$% (1/6)	Yes
		2	Triangular	52,9%	≈50% (3/6)	Yes
		3	Step-Ramp	29,1%	≈25% (2/8)	Yes
		4	Saccades	Not performed	–	–

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