Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 December 2020 doi:10.20944/preprints202012.0388.v1

Article

Gaze following and pupil dilation as objective measures of early diagnosis of children with ASD

Raquel Camero [1], Verónica Martínez [1]* and Carlos Gallego [2]

[1] Department of Psychology, University of Oviedo; uo217941@uniovi.es martinezveronica@uniovi.es
[2] Department of Experimental Psychology, Complutense University of Madrid; carlosgallego@ucm.es
* Correspondence: martinezveronica@uniovi.es ; Tel.: +34-985104107 (VM)

Abstract: (1) Background: Children with autism spectrum disorder (ASD) show certain characteristics in visual attention which generate difficulties in the integration of relevant social information to set the basis of communication. Gaze following and pupil dilation could be used to identify signs for the early detection of ASD. Eye-tracking methodology allows objective measurement of these anomalies in visual attention. The aim is to determine whether measurements of gaze following and pupillary dilation in a linguistic interaction task, captured using eye-tracking methodology, are objective for early diagnosis of ASD. (2) Methods: 20 children between 17 and 24 months of age, made up of 10 neurotypical children and 10 children with ASD were paired together according to chronological age. A human face on a monitor pronounced pseudowords associated with pseudo-objects. Gaze following and pupil dilation was registered during the task. (3) Results: Significant statistical differences were found in the time of gaze fixation on the human face and on the object, as well as in the number of gazes. Also, there were significant differences in the maximum peak of pupil dilation, this being found in the neurotypical group at the moment of processing of the pseudoword, and in the ASD group in the baseline prior to the task (4) Conclusions: The registration and the duration of gaze, and the measurement of pupil dilation with 'eye-tracker' are objective measures for early detection of ASD.

Keywords: language acquisition; Autism; eye-tracker; Pseudowords; pupil dilatation; gaze following

---

1. Introduction

From an early age, babies show a preference for maintaining visual contact with their parents and directing their attention towards the human voice and relevant social stimuli [1]. The fact that they pay attention to the eyes and the mouth of the people who interact with them allows babies to construct social knowledge, fundamental to their neurological development and the learning of language [2]. Evidence exists that the contact and gaze following act as a precursor to the acquisition of overall attention abilities, the imitation and the acquisition of new knowledge and cognitive abilities which are fundamental in language development [3].

Autism spectrum disorder (ASD) is a neurological development disorder characterised by emotional and social difficulties, together with problems of communication and interests and patterns of restricted behaviour. Children with ASD show difficulties when attending to socially relevant areas of the face, and, as a consequence, they do not adequately analyse gestures and social information from others, or different social situations. They appear to have difficulty when acquiring basic social knowledge that neurotypical children learn easily [1]. This specific deficit for paying spontaneous attention to that which is socially relevant, and to the activities of others is present in these children from the first year of life. Due to this, visual attention could serve as a phenotypical characteristic for identification and diagnosis of children at risk of having ASD, before reaching one year of age [4]. The use of eye-tracking methodology for the diagnosis of ASD is widely documented

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 December 2020 doi:10.20944/preprints202012.0388.v1

[5]. Recent research has observed that eye movements and the reactions to verbal/visual stimuli used in eye-tracking methodology could be used as signs of early diagnosis of ASD [6, 7].

Therefore, studies carried out with this methodology, which allows measurement and objectivization of which zones a person directs their attention to during a certain task (gaze following), have found that children with ASD, in comparison with neurotypical children, spend a lot less time paying attention to those areas relevant to social communication, such as the eyes and the mouth [8-10]. Furthermore, it has been observed that eye movements in children at risk of autism, between six and nine months, show significantly lower gaze fixation in comparison with the neurotypical group [11]. Babies that carry out shorter gaze fixations were afterwards diagnosed with autism at 36 months of age.

Also, it has been observed that children of two years diagnosed with ASD show greater preference for fixing their attention on geometric figures than on human faces [2]. Equally, significant differences have been found in children with ASD, with respect to neurotypical children, in changes in gaze during a word processing task, given that the former do not move their gaze towards an object when they hear the word [12].

Recent studies maintain that, apart from an affectation in gaze following, there exists an atypical regulation in the autonomic nervous system (ANS) in children with ASD, which may be contributing to the difficulties that they show in social processing. A reliable measure for studying this atypical regulation would be pupil dilation, given that babies are capable of controlling eye movements from four months of age [13].

Anderson et al. [14] studied pupil response to images of faces and non-faces in children with ASD and found that these showed pupil constriction as a response to images of children's faces, while neurotypical children showed pupil dilation in response to the same stimuli. Years later, the same authors [15], using the same methodology included a base line measure, and observed that the group of children with ASD showed greater pupil dilation at that moment in comparison to the neurotypical group. These results are in line with the theory of the existence of a high level of arousal in children with ASD. In this same direction, Martineau et al. [16] observed different behaviour patterns in a group of children with ASD compared to neurotypical children on visualising slides of faces, avatars and objects. While the neurotypical group had a significant decrease in pupil size when they had already been shown the stimuli, in the children with ASD high pupil dilation was observed during the entire experimental situation, which seems to indicate atypical functioning of ANS. Other studies also support this hypothesis [11, 17-19]; a high level of arousal could be atypical, giving rise to more invariant patterns of gaze and visual movements. Furthermore, this variable seems to be related to frequent sleep problems which are suffered by children with ASD [20]. From a cognitive point of view, a relatively low and appropriate level in the situation of arousal, facilitates adequate processing of social information.

This study aims to test the use of *eye-tracking* methodology as a measure for early detection of ASD in a communicative interaction task. Currently, as far as we know, measures do not exist which allow objectifying and making an early diagnosis of these disorders in Spanish from a linguistic processing task. *Eye-tracking* is a non-invasive and relatively economical methodology that allows children of very early ages (less than 12 months) to be detected as having a high risk of ASD, and, consequently, to begin early intervention, which will be translated into better quality of life for the parents and children affected by this disorder.

Therefore, the first objective will be to compare the gaze following of children with ASD and neurotypical children (NTD) when they hear a pseudoword emitted by a human face. The hypothesis is that those children with NTD will fix their gaze on the human face a greater number of times, specifically on the eyes, except on hearing the pseudoword, when visual attention is fixed on the mouth. On the other hand, patterns of visual attention in children at risk of autism will be more inconsistent, fixing their visual attention a greater number of times on the object and ignoring or paying very little attention to the human face.

A second objective will be to compare the size of pupil dilatation in both groups when they hear the pseudoword. The hypothesis, supported by other studies previously cited, is that the pupil

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 December 2020 doi:10.20944/preprints202012.0388.v1

dilation in children with NTD will increase when the pseudoword is presented, while in the case of children at risk of having ASD, the greatest dilation will be seen at outside the linguistically relevant moment and anomalous patterns of dilation and constriction, contrary to the neurotypical group, will be produced, due to their difficulties of selective attention to the relevant information for communication.

2. Materials and Methods

Participants

The sample was made up of 20 Spanish participants. Of these, 10 individuals were diagnosed with ASD (1 girl and 9 boys), with an age range of between 17 and 24 months (M = 21 and SD = 2.357) and another 10 individuals with neurotypical development (NTD) (3 girls and 7 boys), with an age range of between 17 and 24 months (M = 20 y SD = 1.944) and without any notable problems or alterations. All of the participants normally attend Preschool in a region in the north of Spain.

The children with ASD were referred by the Early Attention Unit service, in the location where referral was made to this specific Unit for the treatment of autism 'ADANSI' (Association of people with autism '*Silent Children*'). The criteria for selection of the children at risk of autism was: children aged between 17 and 24 months with diagnostic reports of autism from the Neuropediatric Service, and in accordance with the following criteria: significant language delay, scarce visual contact, lack of response when called by name (without hearing problems), low communicative intention and scarcity or lack of capacity to imitate. Furthermore, a protocol of previous evaluation to confirm an ASD diagnosis was applied to the entire sample. This consisted of three tests: the Revised M-CHAT questionnaire (M-CHAT-R/F) for the detection of autism in small children with a follow-up interview [21], the Brunet-Lezine Scale (PY.BL.R) of psychomotor development in early infancy [22], and the Scale of Observation for the Diagnosis of Autismo-2 (ADOS-2)- Module T or Module 1 [23]. The entire sample of ASD children met the established diagnostic criteria.

Table 1 shows the scores of the ASD group and the NTD group on the three scales that make up the evaluation protocol for the confirmation of the diagnosis. Both the chronological age of the participants and the global development age on the Brunette-Lezine Scale is in months and all the participants with ASD show a global age under that for their chronological age. Furthermore, these show a score for diagnosis of autism of 14 or more in ADOS, which indicates a high risk of ASD, while the NTD participants show a score of between 0 and 9. Finally, in the M-CHAT questionnaire, the total scores of the ASD group range between 8-20, which indicates a high risk of ASD, while this ranges from 0-1 in the NTD group.

Table 1. Scores of participants with ASD and NTD in the three diagnostic tests.

Group	Participant	Brunette-Lezine		ADOS	M-CHAT
		Chronological Age	Global Age of Development		
	1	17	10	22	15
	2	21	18	14	8
	3	20	12	21	10
	4	18	9	22	12
	5	22	18	22	15
ASD	6	24	18	20	20
	7	24	16	22	8
	8	20	18	15	9
	9	21	12	21	10

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 December 2020 doi:10.20944/preprints202012.0388.v1

	10	23	12	20	11
	1	18	18	2	0
	2	20	21	0	0
	3	20	20	6	0
	4	17	18	9	1
NTD	5	22	24	8	0
	6	24	24	2	0
	7	20	21	0	0
	8	20	20	0	0
	9	19	18	4	1
	10	20	20	6	0

The neurotypical sample was taken from the first year of Preschool at an Early Education School in the same location. At the beginning of the school year, the centre sent an information letter to all the families of the children in the course for children of 2-3 years of age.

The research design was approved by the Ethics Committee for Research of the University of Oviedo. The study was developed in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for experiments involving human subjects in research and the Spanish Law of Personal Data Protection (15/1999 and 3/2018) principles. The data collection was covered by a written informed parental consent, obtained for all participants.

Procedure

Gaze following (fixing and duration of gaze) and pupil dilation of the participants measured through the pupil diameter was registered during the task which emulated a communicative situation of acquisition of language, in which the emission of words by a human face in association with objects was observed. On a screen, a real face says a pseudoword at the same time as a drawing of the pseudo-object (non-existant invented object) appeared.

The task consisted of nine tests, where the first two were for training. Each of these began with a blue screen, a neutral colour which does not influence the child's pupil dilation, and with a fixation point to direct the child's attention to the centre of the screen. This point, which was maintained for two seconds, corresponds to the baseline of the task. Next, a pseudo-object appeared and emitted an attention-getting sound, and it remained still in the centre of the screen. On remaining still a female face appeared which asked the question: "*What is that*?" with happy and surprised intonation. Immediately following this, the face said the name of the pseudo-object (a pseudoword).

After hearing the pseudoword, the image of the pseudo-object remained on the screen for two seconds, this is supposed to be the fading and processing time of the pseudoword. After this, the drawing of the pseudo-object disappeared and only the face remained, saying "*It's back! And what is it called*?" The face maintained for another two seconds.

To record information, an *eye-tracker* apparatus, Tobii Spectrum 600 Hz, was used. The participants sat in the laps of their parents in front of a 16" monitor with a panoramic aspect ratio of 16.9 in a dark soundproof room. Their central vision was lined up with the centre of the monitor, at a distance of 60 cm between the eye and the monitor. Once the participant was in place, a calibration of 5 points was carried out through colourful and attractive cartoons. This way, luminosity was controlled to ensure that changes in pupil dilatation were due to the task itself and not due to changes in the light. To do this, a photometer MASTECH MS6612 was used, with the criterion that luminosity did not pass 110 lumens.

A group of nine pseudowords was selected from a list of test items MEMOFON [24]. Of these, two were for training purposes (*Muz and Norba*). The pseudowords were differentiated by their complexity both in number and in the type of component syllables. Therefore, two monosyllabic

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 December 2020 doi:10.20944/preprints202012.0388.v1

pseudowords were selected, one phonologically simpler with a consonant+vowel pattern (CV) (*Sel*) and another more complex one with a closed syllable (*Tron*); two pseudowords with two syllables, one more simple (*Sina*) and another more complex since it contains an inverse syllable (*Pamul*); and two pseudowords of three syllables, an easier one (*Bésica*) and another more phonologically complex one (*Calcemar*). Each pseudoword was presented in association with a drawing of the pseudo-object, an invented object. The pseudo-objects were designed specifically for the experiment and were randomly associated with the pseudowords. In the same way, once the pseudowords were associated with the pseudo-objects, the order in which the task stimuli were shown to the different participants was also random. In Figure 1 an example of a pseudoword associated with a pseudo-object can be seen.

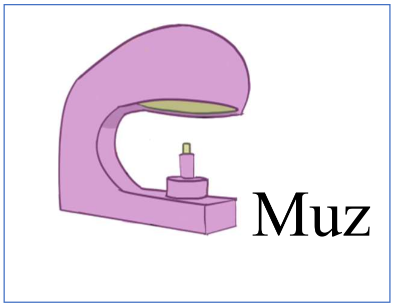

Figure 1. Pseudoword associated with its pseudo-object.

The appearance time of the pseudo-objects and the waiting time between the continuation of the image of the object and the production of the pseudoword was determined based on a pilot study of NTD children aged between 18 and 30 months, in which the same pseudo-objects and pseudowords were used. The times obtained were taken as reference criteria since, in the scientific literature, times are not clearly established for a linguistic processing task using eye-tracking methodology at such an early age.

During the entire task, pupil dilation was registered and measured in millimetres every two milliseconds, as well as gaze and the areas of interest on which gaze was fixed: the pseudo-object (AOI 1), the eyes of the face (AOI 2) and/or the area of the mouth of the face (AOI 3). Data were obtained through the system's software "Tobii Pro Lab": number and time of gazes at the previously defined areas of interest (AOI), and pupil dilation during the whole task.

Data Analysis

The data obtained were analysed with the programme IBM SPSS Statistics – version 22.0 for Windows and the progamme G*Power 3.1. The index for asymmetry and kurtosis were done and a descriptive analysis of the dependent variables (pupil measurement and gaze following) was carried out, as well as of the variable of classification by chronological age (CA). A comparison of means was carried out with a parametric T test of the Student for two independent samples in order to confirm whether difference existed between both groups in the gaze following measurement. Also, a post hoc calculation was done of the size of the Cohen effect (*d*) with the G*Power 3.1 programme to quantify the magnitude of the difference.

On the other hand, an analysis of the variance of repeated measures (ANOVA) was done to analyse the data for intra-group and inter-group pupil dilation. With regard to the analysis of pupil dilation data, a model used by López-Ornat et al. [26] has been followed, thus establishing four periods of measurement. In the first period, during the 400 msg that precedes the start of the task, the baseline (BL) of pupil dilation of each participant measured through the pupil diameter was set. At the same time, the point of gaze fixation was determined [27].

After that, pupil dilation was considered during the time of presentation of the pseudoword (PW). This period was of variable duration due to the different length of the words, between 650 msec and 1,200 msec. The third period corresponded to the following 2,000 msec where measurements

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 December 2020 doi:10.20944/preprints202012.0388.v1

were registered of the period following the fading of the pseudoword (FPW) and the fourth of the video when pseudo-object (PO) and the human face disappeared from the screen, with a duration of two seconds before the next stimulus began. Only the period of presentation of the pseudoword was of variable duration depending on its length. Each of these periods included a set of observations taken every two msec.

3. Results

It can be seen that there are no statistically significant differences between the two groups with regard to chronological age (t(18) = 1.305; p = 0.314). However, there are statistically significant differences with regard to developmental age (t(18)= -4.512; p < .001).

Table 2 shows the kurtosis index (K) and asymmetry (A), the mean (M), the standard deviation (SD), the *t* values, their level of significance and the size of the effect (*d*) in both groups with respect to number and time of gaze fixation on the areas of interest.

Table 2. Mean, standard deviation, differences in means and size of effect in number and time of gaze fixation on the areas of interest between ASD and NTD.

	ASD	NTD	ASD	NTD	ASD	NTD			
	K		A		M (SD)	M (SD)	t	*p*	*d*
NOF	.060	3.515	.971	1.617	135.70 (34.176)	36.70 (10.100)	-8.785	.000	3.928
OFT	-1.513	-.505	-.053	.548	53.62 (7.974)	25.76 (3.141)	-10.281	.000	4.597
NMF	2.571	-.105	1.548	1.138	52.50 (36.391)	4.20 (2.781)	-4.185	.001	1.871
MFT	-1.312	1.140	.720	.64	30.16 (19.998)	2.21 (2.140)	-4.394	.000	.,965
NEF	-.673	.059	-.707	-3.18	32.00 (.978)	209.70 (9.534)	40.718	.000	18.209
EFT	-1.115	5.362	.353	-2.207	20.86 (11.718)	152.83 (15.343)	21.616	.000	9.667

Note: NOF= Number of object fixations, OFT= Object fixation time, NMF= Number of mouth fixations, MFT= Mouth fixation time, NEF= Number of eyes fixations, EFT= Eyes fixation time

With regard to gaze preference, statistically significant differences were observed between the two groups with respect to the number of fixations on a pseudo-object, the eyes and the mouth. The NTD participants showed a clear preference for the eyes in the human face (M = 209.70, and the ASD participants showed preference for the pseudo-object (M = 135.70). Furthermore, the ASD group look at the mouth a greater number of times (M = 52.50) than the NTD group (M = 4.20). As may be observed, the size of the effect on all variables is high ($d > 0.80$).

With regard to the time of fixation, significant statistical differences have also been found ($p < .001$). The NTD participants spend more time concentrating their attention on the eyes of the human face (t = 21.616; $p < .001$), while the ASD participants spend more time observing the pseudo-object (t = -10.281; $p < .001$). Within the human face, the children with ASD centre their attention to a greater

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 December 2020 doi:10.20944/preprints202012.0388.v1

extent on the mouth (M = 30.162) than on the eyes (M = 20.86) in comparison with the NTD group (M = 2.21 and M = 152.83 respectively), both differences being statistically significant ($p < .001$).

For the calculation of pupil dilation, firstly, a prior pruning of the data was carried out in order to exclude missing data or blinking. Afterwards, the mean of pupil dilation was calculated in sections (BL, PW, FPW and PO) for each pseudoword and the total mean of the group of pseudowords was calculated for each section (BL, PW, FPW and PO). Thus, the mean for dilation for the two groups in each section was obtained (Table 3.) It can be seen how this, in general, is higher in children with ASD and, in particular, the greater mean for this group is given in section PO, which corresponds to the moment in which the pseudo-object disappears. With respect to the NTD group, greater dilation was observed in section PW, the moment when the pseudoword is heard.

Table 3. Mean of pupil dilation (mm) for each period in the example.

		BL	PW	FPW	PO
P1	ASD	4.337	3.839	3.776	3.780
	NTD	3.657	3.627	3.593	3.655
P2	ASD	3.677	3.632	3.558	3.596
	NTD	3.392	3.589	3.122	3.272
P3	ASD	3.502	3.696	3.603	3.627
	NTD	3.502	3.636	3.512	3.568
P4	ASD	3.499	3.775	3.492	3.650
	NTD	3.496	3.633	3.572	3.560
P5	ASD	3.514	3.655	3.715	3.762
	NTD	3.680	3.659	3.533	3.546
P6	ASD	3.610	3.608	3.733	3.925
	NTD	3.536	3.596	3.749	3.642
P7	ASD	3.610	3.608	3.733	3.925
	NTD	3.358	3.730	3.713	3.580
P8	ASD	3.772	3.725	3.731	3.844
	NTD	3.618	3.960	3.775	3.586
P9	ASD	3.575	3.803	3.687	3.851
	NTD	3.483	3.520	3.631	3.691
TOTAL	ASD	3.685	3.711	3.659	3.753
	NTD	3.525	3.661	3.578	3.567

Figure 2 shows the behaviour of pupil dilation during the entire task. It can be seen that the ASD participants showed an activation level above that of the NTD participants during all periods. However, the similarity in the evolution of the curve indicates that, although with a greater level of activation, the ASD participants behave in a similar way to the neurotypical participants. Both groups begin with a lower activation level during the baseline (BL), the moment preceding the beginning of the task. Activation increases notably at the beginning of the presentation of the pseudowords (PW) and continues to increase during the task. However, a difference may be observed at the time of presentation of the pseudowords. Here, the NTD participants show a drop, in longer pseudowords, at the end of the presentation of the pseudoword and their activation seems to become stable, while in the ASD group, it continues to increase. Furthermore, the maximum peak of the NTD participants is produced when they are processing the pseudoword and when the waiting time commences (FPW). In contrast, in the ASD group this is produced at the end of the pseudoword (PW) and at the

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 December 2020 doi:10.20944/preprints202012.0388.v1

moment of the object's disappearance (PO). At the end, the period of fading of the pseudoword (FPW) lowers the activation of both groups. When the object disappears and the face says the pseudoword again (PO), activation once again increases in both groups.

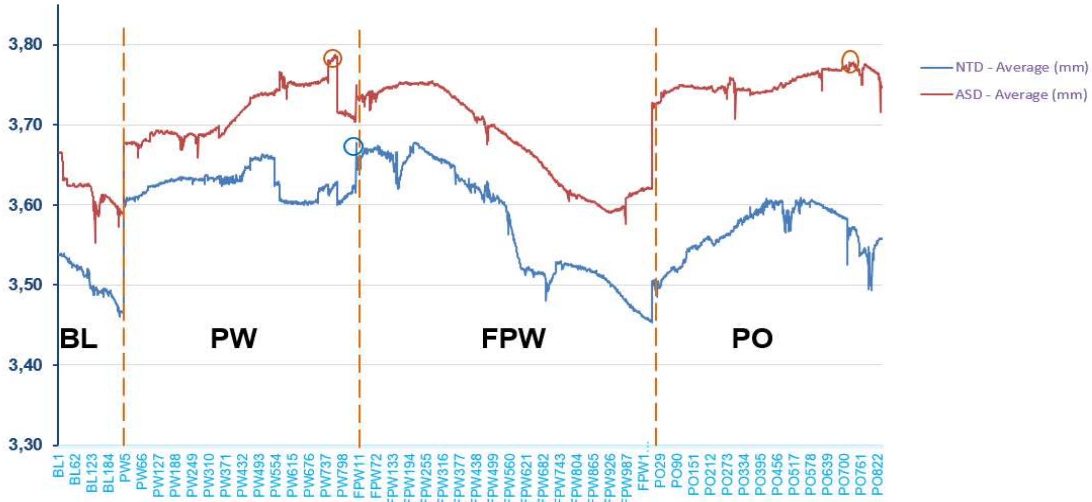

Figure 2. Maximum peak of the complete sequence (in mm)

Following the model proposed by Anderson y Colombo [15], an analysis of the variance of repeated measures (ANOVA) was carried out on pupil dilation. This showed that statistically significant intra-group differences do not exist, both for the ASD group [F (0.60) = 2.90; *p* = 0.614], and for the NTD group [F (1.45) = 2.90; *p* = 0.244]. Therefore, the groups were homogenous.

The comparison between the groups of size of pupil dilation was carried out through a one-way analysis of variance (ANOVA), observing statistically significant differences between both groups between means for pupil dilation [F (2.51) = 2.156, *p*= .002]. In particular, the ASD group (M = 3.701; DT = 0.14) showed a greater average pupil dilation than the neurotypical group (M = 3.59; DT = 0.18).

Moreover, it was calculated whether there existed statistically significant differences in each period o section, and significant statistical differences were observed between the groups for each section. In the baseline section (BL) [F (3385.31) = 3.86, *p* < .001], in the pseudoword section (PW) [F (5494.74) = 3.84, *p*=0], in section FPW [F (1282) = 3.84, *p* < .001], and in the section where the pseudo-object disappears (PO) [F (25835.63) = 3.847, *p* < .001].

4. Discussion

The measurement of gaze following registered through eye-tracking methodology has become an object of study as a possible diagnostic tool for autism spectrum disorders (ASD). The present study has objectively corroborated that, by using this tool, children with ASD show lower attention to human eyes in social interaction [2], which translates into difficulties when integrating social information which is fundamental for cognitive development and acquisition of language, given that adequate eye contact and the ability to follow the gaze of others, are essential for labelling a referent with a certain word. Therefore, the results obtained are in line with the conclusions already made in other studies [11, 12], suggesting the presence of a non-typical control of attention in ASD, reduced general attention to the eyes and mouth and greater attention to non-social elements. This pattern of attention registered through gaze following suggests less access to the source of social information on the part of people with ASD. While NTD children spend most of their time looking at the eyes, the children at risk of ASD spend their time looking at objects, followed by looking at the mouth, these differences being significant. This difference between the groups in the use of gaze following as a clue to social reference for learning words interferes in the acquisition of language.

With the results found here, we can affirm that the measurement of visual following and attentional preference appears to be sensitive when differentiating an ASD gaze pattern with a neurotypical gaze pattern. This may allow us to establish a suspicion of having autism at an early age.

With regard to the measurement of pupil dilation, at the maximum peak of dilation we have not found results in accordance with what Anderson and Colombo set out in their study [15], since these authors found the maximum peak in the baseline section. In contrast, in the present study, this is observed during the processing of the pseudoword and at the beginning of its disappearance. In the ASD participants, two maximum peaks have been considered, since the variation between both periods is practically the same (3.78 y 3.79). These occur during the presentation of the pseudoword (PW) and the period during which the object disappears (PO).

Regarding the measurement of pupil dilation, we obtain statistically significant differences between both groups with respect to the global measurements of pupil dilation and, specifically, between each period. The ASD group shows a greater higher pupil size median than the neurotypical group, which coincides with the results obtained by Martineau et al [16].

Therefore, the results, in accordance with previous research [18, 19], suggest that children with ASD show an inadequate level of neural activation or low adaptive arousal in the tasks which they must face. The rising level of activation during the task translates into attention level difficulties that could form the basis of the problems that these children have when processing social information in different contexts. In contrast, in the NTD group, maximum dilation was found during the fading and processing of the word, indicating that these children are paying attention and retaining the phonological representation of the pseudoword [26] in working phonological memory, and that they are making a greater cognitive effort at this point in the task. To sum up, they are ready to learn language and to concentrate their interest on this. As for the dilation measurements in different sections, in the children with ASD, the maximum average value is produced during the disappearance of the pseudo-object (PO), which suggests a preference for the object and a lack of attention to key social information and language.

In the present study, eye-tracking methodology has been used in a new way in a linguistic processing task in children of an early age. It has been shown that these types of test could provide evidence when measuring attention bases in the development of the process of acquisition of language in small children, not only after 24 months of age [6] but also before that age. In addition, in comparing NTD children with ASD children, differences are observed in the development of the pattern of gaze during the acquisition of linguistic abilities that appear to have great diagnostic potential.

These findings should be interpreted from a neuro-psychological perspective, since alterations in visual attention are indicative of a state of anomalous neural activation. The results found indicate that indirect, objective measurements of the level of activation, such as pupil dilation (registered through eye-tracking) are excellent candidates for diagnostic indicators of the presence of alterations like ASD. Even so, it would be necessary to carry out a larger future study of the measurements of gaze following and pupil dilation to refine this technique for non-invasive diagnostic screening. It is easy to administer and economical for detection of anomalous gaze patterns in children who could have an autism spectrum disorder.

Author Contributions: R.C., V.M. and C.G. conceived the idea. R.C., V.M., and C.G. conducted the investigation. R.C. and V.M. carried out data curation. R.C. and C.G analyzed data. R.C and V.M. wrote the first draft. All authors read and reviewed the previous version of the manuscript. All authors approved the version to be published.

Funding: This research received no external funding.

Acknowledgments: We appreciate the families who participated in this study. We also acknowledge the Children with ASD Association "ADANSI" of the Principality of Asturias, for their collaboration and involvement. We would also like to thank Guillermo Gallego for the design and drawing of the visual pseudo-objects used in the experiment.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Karmiloff, K.; Karmiloff-Smith, A. Hacia el lenguaje. Madrid, Spain: Morata; **2005**.
2. Shic, F; Macari, S; Chawarsk, K. Speech disturbs face scanning in 6-month-olds who develop autism spectrum disorder. *Biological Psychiat*ry. **2014**, *75*, 231-7. doi: 10.1016/j.biopsych.2013.07.009.
3. D'Souza, D; D'Souza, H; Johnson, MH; Karmiloff-Smith, A. Concurrent relations between face scanning and language: A cross syndrome infant study. *Plos One*. **2015**, *10*. doi: 10.1371/journal.pone.0139319.
4. Chawarska, K; Macari, S; Shic, F. Decreased spontaneous attention to social scenes in 6-month-old infants later diagnosed with autism spectrum disorders. *Biological Psychiatry*. **2013**, *74*, 195-203. doi: 10.1016/j.biopsych.2012.11.022.
5. Howard, P.L.; Zhang, L.; Benson, V. What can eye movements tell us about subtle cognitive processing differences in autism? *Vision*. **2019**, *3*, 22. doi:10.3390/vision3020022
6. Murias, M.; Mayor, S.; Davlantis, K.; Franz, L.; Harris, A.; Rardin. B.; Sabatos-DeVito, M.; Dawson G. Validation of eye-tracking measures of social attention as a potential biomarker for autism clinical trials. *Autism Research*. **2018**, *11*, 166-174. https://doi.org/10.1145/3192714.3192819
7. Frazier, T.W.; Klingemier, E.W.; Parikh, S.; Speer, L.; Strauss, M.S.; Eng, C.; Hardan, A.Y.; Youngstrom, E.A. Development and validation of objective and quantitative eye tracking-based measures of autism risk and symptom levels. *Journal of the American Academy of Child & Adolescent Psychiatry*. **2018**, *57*, 858-866. doi: https://doi.org/10.1016/j.jaac.2018.06.023.
8. Dalton, K.M.; Nacewicz, B.M.; Johnstone, T; Schaefer, H.S.; Gernsbacher, M.A.; Goldsmith HH, et al. Gaze fixation and the neural circuitry of face processing in autism. *Nature Neuroscience*. **2005**, *8*, 519–526. doi: 10.1038/nn1421
9. Klin, A.; Jones, W.; Schultz, R.T.; Volkmar, F.R.; Cohen, D.J. Visual fixation patterns during viewing of naturalistic social situations as predictors of social competence in individuals with autism. *Archives of General Psychiatry*. **2002**, *59*, 809–816. DOI: 10.1001/archpsyc.59.9.809
10. Pelphrey, K.A.; Sasson, N.J.; Reznick, J.S.; Paul, G.; Goldman, B.D.; Piven. J. Visual scanning of faces in autism. Journal of Autism and Developmental Disorders. **2002**; 32:249–261. https://doi.org/10.1023/A:1016374617369
11. Wass, S.V.; Jones, J.H.; Gliga, T.; Smith, T.J.; Charman, T.; Johnson, M.H. Shorter spontaneous fixation durations in infants with later emerging autism. *Scientific Reports*. **2015**, *5*, 1-8. doi: 10.1038/srep08284.
12. Chita-Tegmark, M.; Arunachalam, S.; Nelson, C.A.; Tager-Flusberg, H. Eye-tracking measurements of language processing: developmental differences in children at high risk for ASD. *Journal of Autism and Developmental Disorders.* **2015**, *45*, 3327–3338. doi: 10.1007/s10803-015-2495-5.
13. Verschoor, S.A.; Spapé, M.; Biro, S.; Hommel, B. From outcome prediction to action selection: Developmental change in the role of action-effect bindings. *Developmental Science.* **2013**, *16*, 801–814. doi: 10.1111/desc.12085.
14. Anderson, C.J.; Colombo, J.; Jill, S.D. Visual scanning and pupillary responses in young children with Autism Spectrum Disorder. *Journal of Clinical and Experimental Neuropsychology*. **2006**, *28*, 1238–1256. doi: 10.1080/13803390500376790
15. Anderson, C.J.; Colombo, J. Larger tonic pupil size in young children with autism spectrum disorder. *Developmental Psychobiology*. **2009**, *51*, 207–211. doi:10.1002/dev.20352.
16. Martineau, J.; Hernandez, N.; Hiebel, L.; Roché, L.; Metzger, A.; Bonnet-Brilhault, F. Can pupil size and pupil responses during visual scanning contribute to the diagnosis of autism spectrum disorder in children? *Journal of Psychiatric Research*. **2011**, *45*, 1077-1082. doi: 10.1016/j.jpsychires.2011.01.008.
17. Wagner, A.E.; Toffanin, P.; Bas, K.D. The timing and effort of lexical access in natural and degraded speech. *Frontiers in Psychology*. **2016**, *7*, 398. doi: 10.3389/fpsyg.2016.00398.
18. Nyström, P.; Gliga. T.; Jobs E.N.; Gredebäck, G.; Charman, T.; Johnson M.H.; Bölte S.; Falck-Ytter, T. Enhanced pupillary light reflex in infancy is associated with autism diagnosis in toddlerhood. *Nature Communications*, **2018**, *9*, 1678. doi:10.1038/s41467-018-03985-4.
19. Segers, M.; Bebko, J.M.; Zapparoli, B.L.; Stevenson, R.A. A pupillometry study of multisensory social and linguistic processing in autism and typical development. *Developmental Psychology*. **2020**, *56*, 2080-2094. doi: 10.1037/dev0001090
20. Moore, M.; Evans, V.; Hanvey, G.; Johnson, C. Assessment of sleep in children with Autism Spectrum Disorder. *Children*. **2017**, *4*, 72. doi: 10.3390/children4080072

21. Robins, D.L.; Fein, D.; Barton, M. *The modified checklist for autism in toddlers, revised, with follow-up (M-CHAT-R/F)*. Self-published; **2009**.
22. Josse, D.; Pereda, S. *Brunet Lézine revisado: escala de desarrollo psicomotor de la primera infancia*. Madrid: Symtec. **1997**.
23. Lord, C.; Rutter, M.; DiLavore, P.C.; Risi, S.; Gotham, K.; Bishop, S.L.; Luyster, R.J.; Guthrie. W. *Escala de Observación para el Diagnóstico del Autismo. ADOS-2*. Madrid: TEA. **2005**
24. Mariscal, S.; Gallego, C. La imitación como herramienta para investigar y evaluar el desarrollo lingüístico temprano: Un estudio piloto de repetición de palabras y pseudopalabras. *Revista de Investigación en Logopedia*. **2013**, *3*, 53–75.
25. Cohen, J. *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale, NJ: Lawrence Earlbaum Associates; **1988**.
26. López-Ornat, S.; Karousou, A.; Gallego, C.; Martín, L.; Camero, R. Pupillary measures of the cognitive effort in auditory novel word processing and short-term retention. *Frontiers in Psychology*. **2018**, *9*, 2248. doi: 10.3389/fpsyg.2018.02248
27. Guasch, M.; Ferré, P.; Haro, J. Pupil dilation is sensitive to the cognate status of words: further evidence for non-selectivity in bilingual lexical access. *Bilingualism*. **2017**, *20*, 49–54. https://doi.org/10.1017/S1366728916000651