

Research Article

Eye-Tracking Technique as an Instrument in the Diagnosis of Autism Spectrum Disorder

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Considering the prevalence of ASD, as well as unknown etiology and symptomatic evidences occurring in the first years of life, it is necessary to study more precise techniques, whose purpose is to refine the characteristics of ASD, to present a differentiated diagnosis and, thus, to establish an appropriate prognosis according to conditions presented by the patient. In this regard, the ocular tracking technique allows a better understanding of social cognitive functioning, since the main characteristics of ASD are the deficits in social interactions and social communication. The present research was a bibliographical review, whose objective was to analyze scientific publications on the use of the technique of ocular tracking as an instrument in the diagnosis of Autism Spectrum Disorder (ASD). Method: selecting scientific publications, written in Portuguese and English, between 2006 and 2016, published in PUBMED, Sci ELO, LILACS and CAPES databases, including bibliographic reviews and experimental researches with positive or negative results, in order to collect data on the efficacy of the technique in neuropsychological evaluation in cases of ASD. Results: a total of 23 articles were identified, of which 17 were published in PUBMED database and 6 in LILACS. There was an increase in production between 2012 and 2016. Regarding the type of research, 21 are experimental, whose main objectives were investigating joint attention, social attention and face processing, and 2 bibliographic reviews. Conclusion: the eye tracking technique in the experimental research as a differential in the diagnosis of ASD was efficient to present positive results in confirming diverse patterns used by the ASD group compared to groups of typical development or other genetic syndromes.

Keywords: ASD; Eye Tracking; Diagnostic**Abbreviations**

ASD: Autistic Spectrum Disorder; PUBMED: National Library of Medicine and the National Institutes of Health; SCIELO: Scientific Eletronic Library Online; LILACS: Literatura Latino Americana e do Caribe em Ciências da Saúde [Latin American and Caribbean Center on Health Sciences]; CAPES: Coordination for the Improvement of Higher Education Personnel; FXS: Fragile X; CDLS: Cornelia de Lange; RTS: Rubinstein-Taybi; PRT: Pivotal Response Treatment; ESCS: Early Social Communication Scales; ERP: Event related potencial; TD: Typical developmental; JA: Joint attention; IQ: Intelligence quotient

Background

ASD is classified as a neurodevelopmental disorder. Its occurrence is evidenced in childhood and has as main characteristics the persistent deficits in social communication, social interaction and restricted, repetitive patterns of behavior, interests or activities[1]. The studies about ASD have the purposes of better understanding its etiology, disseminating information that helps the relatives of the patients to detect different behaviors as soon as possible, to inform about possible adjustments of their new special conditions and thus to promote improvements in the quality of life of their patients. The ASD diagnosis is based on interviews with those adults responsible

for the child, on the behavioral observations of the child and on the use of some specific instruments. Due to the positive results, the technique of eye tracking is a great ally [2,3]. The eye tracking technique is classified as a neuro scientific, non-invasive method that provides information about brain functioning through the study of abnormalities in ocular movement, allowing to evaluate time and location of the ocular fixation when looking at the visual stimulus [4]. Applied as an investigative method, it allows to obtain knowledge of the significant characteristics of the ASD, that is, the deficits related to the social cognition associated with the difficulty in facial recognition, identity and hesitation of the eye contact, causing impairment in interpersonal relations [5]. Unlike people of typical development, people with autism do not look at a person or picture of people with their eyes directed at them. Thus, the main objective of this article was to review bibliography on the use of eye tracking technique in neuropsychological evaluation as a differential diagnosis in patients with ASD to verify their efficacy.

Method

Selecting scientific publications, thesis and dissertation, published between 2006 and 2016 (ten years), written in Portuguese and English, focused on the use of the eye tracking technique as a differential diagnosis in cases of ASD, also allowing the quantitative comparison between Brazilian and international publications. The research

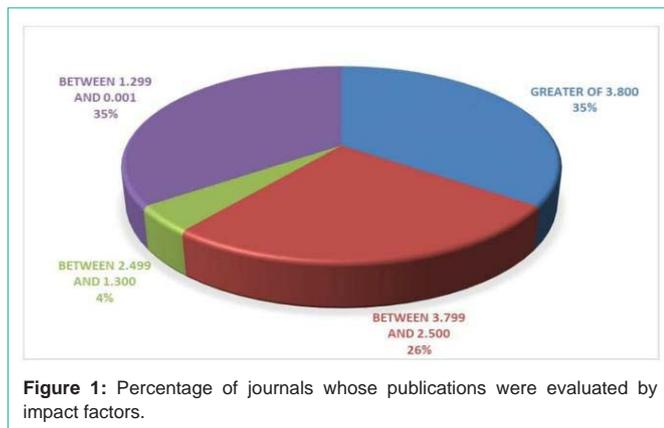


Figure 1: Percentage of journals whose publications were evaluated by impact factors.

included both bibliographic review publications and experimental researches with positive or negative results, with no distinction of the use of the technique at different ages. The databases used were: PUBMED, ScieLO, LILACS and for searching thesis and dissertations CAPES database was used. Autism, ASD, eye tracking, diagnosis and their correlates in Portuguese were the keywords used. As exclusion criteria were considered: repetition of publications in more than one database, publications presenting only abstract and not full text, publications that did not mention the eye tracking technique, ASD, autism and diagnosis and publications out of the specific period of 10 years (2006-2016).

Results

A total of 23 articles were identified distributed as follows: PUBMED: 17 articles, LILACS: 06 articles, according to the pre-established inclusion and exclusion criteria presented in this study and considering the keywords expressed in the titles of the publications. The scientific publications identified in PUBMED database were analyzed considering only the ones written in the English language, regardless of the author's nationality. About the period, between 2006 and 2009 05 articles were published and between 2012 and 2016, there was an increase in production totalizing 18 articles. As for the nationalities, amongst the 17 international publications, the majority is from the United States of America. Regarding the 06 Brazilian scientific publications found, 03 of them were written in English. In total, there were 20 scientific articles written in the English language and 03 written in the Portuguese language. Most of the papers presented experimental research results and only 02 of them were bibliographic reviews.

It was possible to elaborate a systematic chart with the main characteristics of the experimental research publications (Table 1).

In general, the main objectives of the experimental research were to investigate the processing of faces (06 articles), joint attention (05 articles) and social attention (05 articles). As for the method, only 03 articles used a multi-method approach.

Regarding the participants, 14 experiments were performed with groups of participants at high risk or previous diagnosis of ASD versus groups of participants with typical development, 03 experiments had only groups of participants with typical development, 02 only with participants with ASD, and 02 experiments were identified with groups of participants with other genetic syndromes: Rett, FXS, CdLS

and RTS. 01 experiment compared the results between participants with ASD and participants with special needs and 01 experiment analyzed differences in outcomes between participants with ASD, Rett Syndrome and typical development.

Most of the experiments were performed in groups of children (08 experiments), followed by heterogeneous groups regarding chronological ages: adolescents and adults (04 experiments), children, adolescents and adults (04 experiments), children and adolescents (03 experiments). The other homogeneous groups had adult participants (02 experiments), infants (01 experiment) and adolescents (01 experiment).

The periodic impact factor was evaluated according to QUALIS classification, which is the set of procedures used by CAPES in Brazil to stratify the quality of the intellectual production of graduate programs. Figure 1 presents these findings.

Thus, 35% of the journals in which the articles were published showed a greater impact factor of 3.800 and 26% of them had impact factors between 3.799 and 2.500. These percentages indicate that 61% of the journals in which the articles were published had impact factors of journals classified as A1 and A2 (according to Qualis), suggesting that articles have broad exposure in the academic world. On the other hand, 35% of articles were published in journals with impact factors between 1.299 and 0.001, which are classified according to Qualis as B2 periodicals. It is important to note that six of the eight journals included in this classification are Brazilian journals. Journals published in third world countries such as Brazil tend to present low impact factors due to their probable availability of these journals for access in great scientific centers, low priority regarding their subscription to libraries, the preference of researchers to publish their best works in foreign journals with a high impact factor and the tendency in the Brazilian case for many of the researchers not to mention their research colleagues [6].

Discussion

The present review presents data on the scientific studies about the application of the eye tracking technique as a differential in the diagnosis of ASD.

Most scientific publications were written in English and identified in PUBMED and LILACS databases, which suggests greater visibility and international prestige, since such databases are acknowledged as leaders in the availability of studies related to health and with attested quality of information convergent with the journal's impact factor.

About the higher incidence of production in the period between 2012 and 2016, the prevalence of ASD, technological evolution and easy access to the eye tracking technique can be considered as the main findings, stimulating the increase of interest in producing experimental studies.

The investigative character of the experimental research makes broad discoveries about ASD possible, which is vital for its comprehension, given its complexity, and unknown etiology. As an example, the eye tracking technique has been positive in allowing the integration of such results with several investigative methods and establishing significant differences between ASD and other genetic syndromes whose main characteristic is also the impairment in social

Table 1: Description of the articles investigating the eye tracking technique as a tool for diagnosis.

PUBLICATIONS	TYPES AND AIMS OF RESEARCH	PARTICIPANTS	RESULTS
Altered gaze following during live interaction in infants at risk for autism: an eye tracking study [11].	Experimental Aim: To evaluate gaze following in high risk infants compared to typical development ones.	Total: 64 10-months-old infants: 47 high risk ASD e 17 typical developmental.	Compared to the typical development group, diversified patterns were found, especially in the eyes only condition. High-risk infants demonstrated performance impairment when guidelines were reduced.
Eye-tracking as a measure of responsiveness to joint attention in infants at risk for autism [14].	Experimental Aim: To examine construct validity of JA response.	40 18-months-old infants high risk ASD.	It has been shown that both ESCS tasks and eye tracking can be used to evaluate joint attention responses in high-risk infants. However, there was no correlation between the distal ESCS task and eye tracking with language.
Broad autism phenotype in typically developing children predicts performance on an eye-tracking measure of joint attention [15].	Experimental Aim: To develop and validate JA how endophenotypes of ASD.	46 typical developmental children between 03 and 09 years.	Differential patterns in the distribution of the gaze between the two conditions in children with low levels of ASD symptoms were observed: greater time of observation to the target in the congruent condition compared to the incongruous condition and greater distribution of the look to the face of the model in the incongruent condition than in the congruent condition. In contrast, children with high levels of ASD had attenuated differences in the distribution of gaze between congruent and incongruent conditions.
Eye-tracking, autonomic, and electrophysiological correlates of emotional face processing in adolescents with autism spectrum disorder [16].	Experimental. Aim: To examine neural, behavioral and autonomic correlations in face processing, using the eye tracking and ERP.	Total: 38 individuals with ages between 13 and 21 years - 18 ASD e 20 typical developmental.	Eye tracking data demonstrated a similar scanning between groups on emotional faces. ERP measures revealed a lack of neural differentiation between the types of emotion in the ASD group. Regarding autonomic activation, there were no differences between groups in the pupil diameter in responses to emotional faces, but there was an association with increased pupil diameter with longer observation time for the mouth in ASD participants.
Eye-tracking as a measure of receptive vocabulary in children with autism spectrum disorders [17].	Experimental. Aim: To examine the utility of eye tracking technique to evaluate speech comprehension.	Total: 29 children between 42 and 82 months: 14 ASD boys and 15 matched boys with typical developmental.	Differences in looking time were found in the ASD and TD groups. The ASD and TD children, in the known condition, looked longer at target X non-target images. In the unknown condition, the ASD children did not present significant differences in the target X non-target image, but with the TD children there was a significant difference in the looking time of the target X non-target images, which may suggest emerging knowledge.
Atypical visual saliency in autism spectrum disorder quantified through model-based eye-tracking [18].	Experimental. Aim: To investigate the visual attention towards stimuli and their features in ASD individuals.	Total: 39 individual: 20 ASD (mean age: 30.8 +/- 11.1 years) e 19 matched typical developmental (mean age: 32.3 +/- 10.4 years).	Diverse patterns of visual attention were identified in the ASD group: more fixations to the center of the images, even when there are no objects, which can be attributed to the slow speed of the saccadic; increase of fixations in regions with level-pixel influence, but decrease of fixations in regions with influence in the semantic-level (sense of the scene) and level-object; atypical attention to specific semantic objects: slowness to fix on faces, but speed to fix on mechanical and manipulable objects.
Disentangling the initiation from the response in joint attention: an eye-tracking study in toddlers with autism spectrum disorders [19].	Experimental. Aim: To describe the differences in the visual patterns during the both task of JA: responding and initiation.	17 children ASD and 15 children with typical developmental between 18 and 30 months old.	Positive results regarding the use of the eye tracking technique to investigate the JA initiation patterns of atypical developments, being better able to detect differences between ASD and typical development children. Regarding the task of responding JA, there were no differences between groups. As for the tasks of initiation JA there were patterns diversified of fixation and transitions between the groups.
Measuring social attention and motivation in autism spectrum disorder using eye-tracking: stimulus type matters [20].	Experimental. Aim: To investigate social attention with three types of stimuli.	Total: 81 children and adolescents between 06 and 17 years: 59 ASD e 22 typical developmental.	Demonstrated differentiation in visual pattern to social stimuli, apparent when participants with ASD observed dynamic stimuli representing interaction. The task of interactive visual exploration was considered the best to obtain a distinction in the look pattern between the ASD and TD groups. Therefore, it was concluded that the naturalistic validity is a key factor to be considered when using the eye tracking technique in ASD studies.

Abnormality in face scanning by children with autism spectrum disorder is limited to the eye region: evidence from multi-method analyses of eye tracking data [21].	Experimental. Aim: To investigate similarities and differences between groups of ASD and TD in facial processing using a multi-method approach.	3 groups of children: 20 ASD, 21 matched in age typical developmental and 20 matched in IQ typical.	Positive result regarding the differentiation in relation to face processing in the ASD group, suggesting not to be a general abnormality but specific to the eye region: there was significantly poorer face recognition compared to children compatible with age and IQ. In the case of the eye tracking approach to the areas of interest, the ASD children fixed less on the faces than those compatible with age and IQ. As for proportional fixation time in the eyes, nose and mouth, there was no significant difference between groups, but ASD fixed less time in the right eye. Heat maps showed that the fixations of age-matched typical developmental children were focused more on the pupils of both eyes while the fixations of ASD infants were tilted to the left eye and below the eye rather than the pupil region.
Others' emotions teach, but not in autism: an eye-tracking pupillometry study [22].	Experimental. Aim: To investigate the disruption of social-emotional calibration in children with ASD.	40 children between 02 and 05 years: 20 ASD e 20 typical developmental.	There was identification of differentiation in the emotional responses between the groups. The ASD children did not react emotionally to the emotional facial expressions of the actor.
Eye-tracking in early autism research [23].	Bibliographic review. Aim: To review the use of eye-tracking technique in the early diagnosis of ASD.	Method: Review of research focused on the use of eye tracking to identify early autism, mainly research that contributed to the significant advancement of knowledge. Databases: PubMed, Web of Science, Google Scholar. Key words: autism, child, eye tracking. Period: until August 2013.	32 publications were identified and it was concluded that the results obtained by the eye tracking technique point to a diversified pattern of gaze in infants and children. The possibility of being a conceivable technique was considered as an integral part of the screening and diagnostic evaluations, since it is a non-invasive method, ideal for children and babies, which allows the communication of the results to parents and other interested parties.
An eye-tracking method to reveal the link between gazing patterns and pragmatic abilities in high functioning autism spectrum disorders [24].	Experimental. Aim: To examine associations between pragmatic skills and facial processing.	Two experiments: Group (1) 11 typical developmental individual between 24 and 40 years and Group (2) 11 ASD high function individual between 17 and 31 years.	Diverse results were identified between the groups. In the ASD group, there was a positive correlation, that is, the more they looked at facial expressions the more they used cognitive verbs, in contrast, the typical development group, although it increased their observation time to the faces in the contingent viewing window condition, there was no correlation with the proportion of cognitive verbs.
Visual preference for social stimuli in individuals with autism or neurodevelopmental disorders: an eye-tracking study [8].	Experimental. Aim: To explore the differences in visual attention preference social versus non-social stimuli.	Two groups: (1) 16 adolescents with ASD and 16 adolescents with SEN without diagnosis of a neurodevelopmental disorder, matched in chronological age, gender and verbal ability; (2) 15 individual FXS, 14 individual CdLS e 19 individual RTS, matched in chronological age and global adaptive behavior, and verbal adaptive behavior.	It revealed that the results of the use of eye tracking technique were positive to evaluate differences in visual patterns in preference in groups of typical development, ASD and other genetic syndromes that are distinguished by differentiated social behaviors.
Reactivity to fearful expressions of familiar and unfamiliar people in children with autism: an eye-tracking pupillometry study [25].	Experimental. Aim: To identify the emotional reaction to the emotions of family members through facial processing.	Total: 42 children between 2 and 5 years: 21 ASD e 21 typical developmental matched in chronological age and gender.	Differentiated patterns were identified in the reactions of the pupils between the groups regarding the emotional reaction of unknown X relatives. The findings indicate that the ASD group reacted normally to the expressions of fear of the known people and reduced pupillary reactive responses to unknown persons, indicating that there is no widespread emotional impairment in autism.
Eye tracking young children with autism [26].	Bibliographic review. Aim: To provide guidelines.	Methods: Guideline about the use of the eye tracking technique.	It concluded that it is the promising eye tracking technique to identify early emerging mechanisms of ASD development.
Brief report: Broad autism phenotype in adults is associated with performance on an eye-tracking measure of joint attention [27].	Experimental. Aim: To investigate the associations between characteristics of the ASD phenotype and gaze patterns through joint attention.	44 typical developmental adults between 18 and 50 years.	Positive results were found for association between pattern of look and characteristics of the ASD phenotype, both in fixation time and modulation of the gaze, suggesting that measurements obtained by the use of eye tracking may define an endophenotypes.
Visual attention for social information and salivary oxytocin levels in preschool children with autism spectrum disorders: an eye-tracking study [28].	Experimental. Aim: To investigate the relation between visual attention of social preference and levels of oxytocin.	19 ASD children (mean age: 57,9 month) and 60 typical developmental children (mean age: 48,1 month).	Positive correlations were found between the high level of oxytocin and visual attention in fingertip images in children with typical development. It was not found in children with ASD, suggesting the association between oxytocin and visual attention to social information.

<p>The eye-tracking of social stimuli in patients with Rett syndrome and autism spectrum disorders: a pilot study [7].</p>	<p>Experimental. Aim: To compare visual attention in social stimuli of groups with RS, ASD and typical developmental.</p>	<p>14 RS (between 4 and 30 years), 11 ASD (between 4 and 20 years) e 17 typical developmental.</p>	<p>The results were positive in identifying differences in visual patterns to social X non-social stimuli between the RS, ASD and typical developmental groups. RS patients looked longer at social stimuli compared to ASD patients. It has been found that according to advanced age, RS patients tended to decrease the time of visualization to social stimuli. It was concluded that the social impairment characteristic of RS different from ASD.</p>
<p>Perceptual patterns in developmental disorders: eye-tracking for social pictures and non-social pictures [29].</p>	<p>Experimental. Aim: To verify the differences in visual pattern of social X non-social stimuli between ASD participants and TD.</p>	<p>11 ASD individual between 08 and 14 years, matched in chronological age, gender and IQ control-group.</p>	<p>The presented results differences in the visual patterns regarding the organization, dispersion and omission in perception of the social X non-social stimuli in the ASD group compared to the group with typical development. The ASD group presented more omission patterns and used less organized tracing of tracking compared to the group with typical development.</p>
<p>Face perception in children and adolescents with Pervasive Developmental Disorders [30].</p>	<p>Experimental. Aim: To compare the performance of ocular screening in human face figures between ASD and TD children.</p>	<p>10 ASD children and adolescents and 10 typical developmental children and adolescents. Matched groups in chronological age between 08 and 19 years and gender.</p>	<p>The presented results showed different performances of the ASD group compared to the group with typical development in relation to the time of fixation to the stimuli, and the ASD group spent less fixation time on the whole face, less fixation time on the faces and the region of the eyes in the inverted figures and less time of fixation of the face in the figures with the hidden eyes.</p>
<p>Concepts of color, shape, size and position in ten children with Rett syndrome [31].</p>	<p>Experimental. Aim: To evaluate the recognition of concepts in children with RS.</p>	<p>10 RS children between 4 years and 8 months and 12 years and 10 months.</p>	<p>The presented results suggest that there was no recognition of the basic concepts presented, considering the fixation time of the gaze during the experiment.</p>
<p>New possibilities on neuropsychological assessment in pervasive developmental disorders: analyses of eye movements [3].</p>	<p>Experimental. Aim: To investigate the possibility to use eye tracking technique as a neuropsychological evaluation tool.</p>	<p>10 ASD children and adolescents and 10 typical developmental children and adolescents. Matched groups in chronological age between 08 and 19 years and gender.</p>	<p>The presented results were positive regarding the contribution of eyes movements to the neuropsychological evaluation, since there were significant differences between groups in both tasks, indicating absence of voluntary attentional regulation, difficulty to initiate an action, as well as to inhibit it and direct it to the target.</p>
<p>Saccadic movements using eye-tracking technology in individuals with autism spectrum disorders: pilot study [32].</p>	<p>Experimental. Aim: To verify visual scanning on social and non-social stimuli in participants with ASD.</p>	<p>10 ASD individuals between 4 and 41 years and 10 matched in chronological age typical developmental individuals.</p>	<p>There were significant differences in the visual pattern used in observing non-social X social stimuli of the ASD group compared to the group with typical development, since the results of the ASD group showed a longer duration of saccadic movements to the social figures and the typical developmental group presented higher numbers of fixations on the figure of the woman wearing cat mask with hidden eyes. These results suggest that the ASD group uses different strategies when exploring social stimuli.</p>

ASD: Autistic Spectrum Disorder; TD: Typical developmental; ESCS: Early Social Communication Scales; ERP: Event related potential; JA: Joint attention; IQ: Intelligence quotient; FXS: Fragile X; CDLS: Cornelia de Lange; RTS: Rubinstein-Taybi

cognition. This indicates versatility in its application allowing abettor understanding on the differences and similarities among those syndromes [7,8].

By way of comparison, Brazilian publications focus on the period between 2006 and 2009, with only one paper published in the year 2015, that is, during the period of the greatest scientific production identified in this research. About the quality of the periodic attested by the impact factor according to the Qualis evaluation, all Brazilian publications were classified as B2 periodicals, that is, the average rank. Even though it does not reach the highest result (A1), it is important to highlight the academic relevance of the publications and the effective contribution to the knowledge about the ASD, since Brazil lacks scientific research and incentives for conducting such research investigations.

Most of the experiments were performed in groups of participants whose age group falls into the category of children,

and its non-invasive character is considered one of the advantages of the eye tracking technique concerning the ease of handling the research with the patients by the researchers, allowing the early diagnosis and facilitating improvements in treatment. Also, most of the comparisons of the results obtained in experimental research have occurred between groups of participants with ASD and typical development, which may reinforce the idea of the need to understand the atelicity in the way ASD subjects function.

Although the diagnosis of ASD can be confirmed from the 3rd year of life, it is possible to identify signs between 12 and 24 months [9,10]. In this sense, we highlight the use of the eye tracking technique with the objective of evaluating joint attention, since it is observed in typical development from 9 to 14 months and there was positive evidence regarding the diversified visual pattern in the participants at high risk of ASD of 10 months of age, although, until then, there has been no confirmed diagnosis [11].

The publications identified had positive results of the application of the eye tracking technique as a differential in the diagnosis of ASD. Thus, according to what has been investigated, it is an efficient technique in fulfilling its investigative role on the way ASD works in relation to social cognitive impairment. Based on these findings there is the possibility of assigning diagnostic identification markers.

In that sense, recently, another relevant contribution of the use of the eye tracking technique was reported regarding the possibility of social visual engagement to be considered an endophenotypes of neurodevelopment, not only in ASD, but also in variations of the social information of the population in general [12]. These results suggest genetic influence by triggering mechanisms of seeking and evaluation of social information, confirmed by analyzing the data obtained through the eye tracking technique of the individual experiences of groups of monozygotic and dizygotic twins when visualizing social stimuli. The importance of these findings may indicate new investigative paths on the interaction between the effects of genetic and environmental factors, contributing to increasingly effective interventions.

Given this scenario, there is a research in progress in the United States of America, currently under recruitment, aiming to evaluate the effects of PRT from the implementation of the eye tracking technique in children aged 4 at 7 years with ASD during the 16-week treatment period [13].

In summary, the eye tracking technique showed to be an efficient investigative method to present empirical results of the way the ASD works, being an ally in its early and accurate diagnosis, which favors effective interventions. However, further studies are recommended including multi-method approaches, with interactive stimuli or closer to real situations with homogeneous groups of participants, with compatible chronological age and developmental level to avoid contrasts between results.

Conclusion

It is possible to conclude that the use of the eye tracking technique has been proved to be a differential instrument in the diagnosis of ASD once it can be an efficient method of investigating the functioning of the cognitive processes. This technique presents positive results regarding the significant differences in the visual patterns of neurotypical subjects and with ASD, and the findings that can be related to deficits of social cognition may contribute to the definition of a specific marker of diagnosis. Still, being a non-invasive method and its easy handling characteristic allows the use in infants and children, resulting in early and accurate diagnoses, consequently, in more targeted and effective interventions to improve the development of the patients with ASD, and thus their quality of life.

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