#### REVIEW



# Are early visual behavior impairments involved in the onset of autism spectrum disorders? Insights for early diagnosis and intervention

Fabio Apicella<sup>1</sup> · Valeria Costanzo<sup>1</sup> · Giulia Purpura<sup>1</sup>

Received: 3 September 2019 / Revised: 18 November 2019 / Accepted: 23 December 2019 / Published online: 4 January 2020 © Springer-Verlag GmbH Germany, part of Springer Nature 2020

#### Abstract

A correct use of the visual behavior (VB), and its integration with motor function, represents the earliest mean used by infants to explore and act on the social and non-social surrounding environment. The aim of this mini review is to present influential evidence of abnormalities in the VB domain in ASD individuals and to discuss the implication of these findings for early identification and intervention. We analyzed the possible anomalies in oculomotor abilities, visual attention, and visual-motor integration, as parts of a wider visual behavior defect, that could affect children with autism spectrum disorders (ASD) since the early stages of development.

*Conclusion*: According to the literature, difficulties in these three areas have been often reported in children with ASD, and the visual-perception deficit could have cascading effects on learning processes and on social development. Despite this evidence of atypical VB in ASD, their investigation is not yet included into diagnostic processes, and they are not yet considered a specific treatment target.

#### What is Known:

•Atypical social use of visual behavior is one the first symptoms in children with autism spectrum disorders

•Individuals with autism spectrum disorders often show unusual visual exploration of the surrounding environment

- What is New:
- •It is possible to hypothesize that early visual behavior abnormalities may affect experiences that permit learning processes and social and communicative development in infants
- •An early assessment of visual behavior, as a core symptom of ASD, might improve the diagnostic processes and might help to developing more individualized treatments.

Keywords Autism spectrum disorders · Oculomotor abilities · Visual-behaviors · Visual attention · Visual-motor integration

### Abbreviations

ASD	Autism spectrum disorders
ADOS-2	Autism Diagnostic Observation Schedule-2
BAP	Broader autism phenotype
f-MRI	Functional-magnetic resonance imaging
IJA	Initiation of joint attention

Communicated by Peter de Winter

Giulia Purpura g.purpura@fsm.unipi.it

> Fabio Apicella f.apicella@fsm.unipi.it

Valeria Costanzo v.costanzo@fsm.unipi.it

<sup>1</sup> Department of Developmental Neuroscience, IRCCS Stella Maris Foundation, viale del Tirreno 331, Calambrone, Pisa, Italy

RJA	Response to joint attention
TD	Typical development (adolescents or children)

VB Visual Behavior

# Introduction

Autism spectrum disorder (ASD) is an early onset and lifelong neurodevelopmental disorder characterized by high symptom heterogeneity. Despite the term "spectrum" suggests that the clinical features widely vary among individuals, the core symptoms of ASD affect the social interaction and communication, with the presence of restricted and repetitive patterns of sensory-motor behaviors and interests [2]. Since there are no reliable biomarkers of ASD, the diagnosis is based upon the observation of behavioral symptoms. Several standardized tools have been

developed to help clinicians with the diagnostic process; at the moment, the Autism Diagnostic Observation Schedule-2 (ADOS-2, [28, 29]) is considered the gold standard instrument for the diagnosis of ASD. The ADOS-2 is a semi-structured observation that addresses some target behaviors considered relevant for the clinical diagnosis of ASD. The ADOS is divided into 5 modules, according to the age and the language level of individuals suspected to have ASD, and it can be used from the infancy to the adulthood. While the diagnosis is currently made between 3 and 4 years of age [4], the first behavioral markers begin to emerge at the end of the first year of life; these early behaviors include the reduced visual attention to social stimuli, the atypical object use and exploration, the reduced use of gaze and other non-verbal behaviors to communicate with a social partner, and the difficulty in disengaging and shifting visual attention [25, 30].

Visual behavior (VB) impairments are considered crucial in the wider domain of perceptual impairments that characterize the phenotype of ASD. The VB includes all the processes underlying the ability to pay attention to external stimuli through the gaze and to integrate visual information with motor function in order to act on the environment and adapt to it [27].

From the first days of life, the VB represents the primary means of perceiving and exploring the surrounding world and giving it a meaning in order to guide the action. Early VB impairments could disrupt the development of the ability to learn from the environment and carry out the tasks of everyday life; for this reason, they are supposed to be the first signs of atypical neurodevelopment and their role in the onset of ASD is currently debated [11, 22]. Nevertheless, there is still little information about the links between a potential early VB vulnerability and the subsequent onset of sociocommunicative difficulties and behavioral stereotypes.

Atypical eye contact is one of the most distinguishable manifestation of a qualitative impairment in the social oriented visual-perceptual domain in ASD, but its onset is clearly detectable only after the first year of life [38]. The question on the possible antecedents of the atypical eye contact within the VB domain still remains open; during the early stages of life, it can be assumed that, VB anomalies might include atypicalities in those visual competences leading to the ability to attain the gaze of another person. For this reason, in this brief review, we consider difficulties in (i) oculomotor abilities, (ii) visual attention, and (iii) visual-motor integration, as possible antecedent of social symptoms in VB domain that could affect the perception of social and non-social stimuli (see Table 1).

Discover the role of VB impairments in determine ASD core symptoms should serve the purpose of implementing procedures for early diagnosis and, possibly, of gaining new useful insight to personalize interventions.

#### **Oculomotor abilities in ASD**

The oculomotor system is fundamental for development of the voluntary behavior, and for this reason, its maturation is considered as paradigmatic of brain maturational processes. Mainly, different types of eye movements allow different behavioral and cognitive processes. In particular, slow eye movements supports voluntarily foveation of a stimulus that is moving, while visually rapid movements require the simple, reflexive foveation of a visual target, which allows basic aspects of attention and sensorimotor control [31]. The presence of possible anomalies in eye-movements dynamics, since the early period of infancy, can be suspected as a life-span factor influencing visual-perceptual functions.

As regards rapid eye movements, saccades are defined by their high velocity, precision, and accuracy; these characteristics are necessary for optimal vision, because they position a target of interest on the fovea for high definition vision [49]. During the learning from the environment, the frequency, the amplitude, and the latency of saccadic movements may reflect capacity to detect and assign appropriate saliency to stimuli. For this reason, these parameters are important for many cognitive processes, such as reading and visual search. In particular, saccades frequency, that is the number of saccades for second, seems to reflect the capacity of visuospatial attention and increases slightly with age [40], the amplitude regards the size of the saccade and determines their accuracy, while the latency refers to the reaction time to initiate an eye movement and decreases exponentially from birth to approximately 14-15 years of age when it stabilizes throughout adulthood [31].

A wide line of research has tried to identify whether anomalies in rapid eye movements were specific for ASD, or a more general hallmark of a neurodevelopmental disorder; they analyzed the regulation of saccadic movements and suggested possible correlations with cerebral dysfunctions [17, 26, 33, 34]. One of the pioneer studies on saccadic abnormalities in ASD was performed by Kemner and colleagues [26] by measuring eye-movements frequency in response to three types of stimuli, differentiated on the basis of their recurrence (frequent, rare, and novel). The saccadic frequency in ASD children seemed to be independent on stimulus type, in contrast with both typical developing children and children with attention disorders and dyslexia. Furthermore, children with ASD showed more saccadic eye movements in reaction to frequent stimuli and between stimulus presentations, while typical children showed more saccadic activity during the presentation of novel stimuli. Given the role of the superior colliculus in the generation of saccades, the authors suggested that could be a basic dysfunction of this subcortical area [26]. The possible consequence might be that ASD individuals fail to regulate saccades frequency in order to learn from environment.

Saccadic movements testing were also considered by Goldberg and colleagues [20] as a mean to highlight neural

### Table 1 Overview of recent influential studies on ASD visual behavior

	Age (years)	Method	Main results
Oculomotor abilities			
Kemner et al. [26]	10	Gaze recording during frequent and infrequent visual stimuli.	Children with ASD showed more saccadic eye movements in reaction to frequent stimuli and between stimulus presentation, while typical children showed more saccadic activity during the presentation of novel stimuli
Goldberg et al. [20]	12–18	Eye movements recording on anti-saccade, memory-guided saccade, predictive saccade and gap/overlap tasks.	Children with ASD showed higher percentage of directional errors on the anti-saccade task, higher per- centage of response suppression errors on a memory-guided saccade task and lower percentage of predictive eye movements on a predictive saccade task.
Takarae et al. [53]	8–adults	Pursuit eye movements recording during ramp and oscillating target tasks.	Individuals with autism had normal pursuit latency, but they had deficits in the initial open-loop stage of pursuit only when targets moving in the right hemifield and a bilateral poorer closed-loop pursuit gain.
Pensiero et al. [39]	5–12	Saccadic movements recording toward light stimuli	Lack of saccadic movement alterations in children with ASD but presence of tracts of saccadic initiation failure, continuous changes in saccadic velocity profiles, and instability of fixation.
Mosconi et al. [34]	Adults	Intrasaccadic target step paradigm to study saccade adaptation.	Individuals with ASD adapted slower than healthy controls and demonstrated more variability of their saccade amplitudes across trials prior to, during and after adaptation.
Wilkes et al. [57]	6–12	Eye-movements recording during saccade and smooth pursuit tasks	Abnormal visual smooth pursuit on the vertical plane and a greater latency for initiating saccades in the ASD group
Visual attention			
Van der Geest et al. [54]	10	Saccadic gap-overlap paradigm toward light stimuli	Differences in ASD group about latencies between the overlap condition and the gap condition
Chawarska et al. [9]	2	Visual attention toward eye movement and a nonbiological movement	ASD children with autism had significantly shorter saccadic reaction times to peripheral targets as compared with controls only when presented an eye-movement cue
Chawarska et al. [10]	2-4	Attentional bias associated with faces and non-facial stimuli	Controls had more difficulties disengaging visual attention from faces but not objects than children with autism
McPartland et al. [32]	12–16	Visual attention toward passive viewing of images of human faces, inverted human faces, monkey faces, and geometric figures	Individuals with ASD obtained lower scores on measures of face recognition but exhibited similar patterns of visual attention. In individuals with ASD, face recognition performance was associated with social adaptive function.
Groen et al. [23]	1–5 + parents	Visual scanning recorded during four simple movies that did not feature people	Visual scanning differences between children with autism and control children. Higher ADOS scores is related to more abnormal watching behavior. Atypical visual scanning also in the mothers.
Vivanti et al. [55]	3–5	Visual attention toward an agent's face in order to predict imminent action	Children with ASD failed to show changes in their attention pattern in response to the agent's goal-directed gaze behavior.
Billeci et al. [6]	1.5–2.5	Visual patterns during joint attention task	No difference between ASD and TD groups in responding to joint attention task, but toddlers with ASD in the initiating joint attention task, showed different pattern of gaze transitions and fixations compared to the controls
Murphy et al. [36]	8–13	Attentional bias to non-social visual salience during f-MRI scan	ASD individuals showed atypical reactions to the salience of non-social stimuli.

Table 1 (continued)

	Age (years)	Method	Main results
Visual-motor integration			
Radonovich et al. [44]	3–15	Systematic assessment of postural and motor control (magnitude of postural sway)	Both the overall intensity and frequency scores on the repetitive behavior scale-revised measure were signif- icant predictors of center of pressure sway area in ASD.
Miller et al. [33]	8–15	Dyspraxia and oculomotor tasks	Significant differences between ASD and typically developing children across a broad range of motor tests, including measures of simple motor skills, praxis, saccadic eye movements, motor coordination and visual-motor integration.
Sharer et al. [51]	10	Serial reaction time task to examine visuomotor learning and f-MRI analysis	Differences in neural recruitment during visuomotor learning, particularly within the initial stages of this learning processing.
Sharer et al. [50]	Adults	Serial reaction time task to examine implicit motor skills learning	ASD participants under-utilize visual input during motor learning.
Purpura et al. [43]	5–13	Checklist on visuomotor abilities	Deficits in several motor tasks, above all in a dynamic and unpredictable environment. A greater intensity and frequency of repetitive behaviors in children with motor difficulties.
Nebel et al. [37]	8–12	Gesture examination and resting-state f-MRI analysis	Relationship between the deficit in the ability to combine gestures and the visual-motor connectivity

basis of ASD. Different saccade tasks were administered to high-functioning ASD adolescents and with typical development (TD) adolescents to assess the contribution of different cortical areas for the emergence of VB impairments. Specifically, they recorded eye movements on anti-saccade, memory-guided saccade, predictive saccade, and gap/ overlap tasks to define the accuracy differences in the two groups. The anti-saccade task probes the ability to exert a cognitive control of behavior by exerting voluntary response inhibition because subjects must voluntarily inhibit a reflexive eve movement toward a visual stimulus and instead make a planned movement to its mirror location. The memory-guided saccade task is a sensitive measure of developmental change in spatial working memory, because a peripheral target is briefly presented at an unpredictable location in the periphery while the subject fixates a central target. Subjects must retain fixation and simply remember the location of the probe, and successively they make a voluntary saccade in the absence of a visual stimulus to the remembered location. The predictive saccade task allows understanding the functioning of frontal and prefrontal systems, because the subjects are required to look back and forth between two alternately illuminated lights such that the eye arrives to the position of the light just as it comes on (so the saccade must begin before the light appears). Finally, gap/overlap task is also used to assess the contribution of the parietal system in order to look indirectly at the ability to disengage attention (fixation target extinguished before, simultaneously or after new peripheral target appeared) [20, 31].

In the anti-saccade task, Goldberg and colleagues [20] found a higher percentage of directional errors in ASD adolescents that looked toward stimuli instead of their mirror location as expected by the task. Similarly, ASD adolescents failed to inhibit immediate eye-responses in the memoryguided saccade task in a significant higher number of trials. Directional errors in the first task and inhibitory dysfunction in the second task may be interpreted as a difficulty to suppress unwanted eye-movements, depending on the neural circuits called into action. Finally, in the predictive saccade task, authors reported a greater percentage of predictive saccades for the comparison group compared with the ASD group, suggesting that ASD individuals could not consistently move their eyes within the time window preceding an expected appearance of a stimulus. According to the authors, these kind of diffused abnormalities in oculomotor functioning in patients with ASD provide evidence of the involvement of a number of brain regions, including dorsolateral prefrontal cortex, parietal cortex, and basal ganglia.

While a relationship between atypical saccade dynamics and altered strategies for the exploration of the surrounding environment in ASD is sustained by several studies, it is not completely clear which part of the saccadic sequence contribute to the defect in the visual exploration. Pensiero et al. [39] recorded saccadic movements toward light stimuli presented at 5 to 25 degree of amplitude in the visual field in a group of children with ASD, compared with matched children with typical development. This study, aiming to use eyemovements recordings to assess the saccadic parameters as the amplitude, the velocity, and the latency found no difference in ASD children compared with the control group concerning to the considered parameters. Nevertheless, authors reported frequent period of stillness in ASD children, leading to saccadic initiation failure and to an increase of the number of blinks before and during fast eye movements. Authors, moreover, noted that these saccadic initiation failures are very similar to those observed in the oculomotor apraxia, and suggested that this atypia could be due to a functional alteration of the brainstem reticular formation.

Beside the cerebral areas discussed above, the role of the cerebellar networks in the programming and controlling the precision of eye-movements has to be considered as well.

Starting from evidence of cerebellar vermis abnormalities as results of several post-mortem and neuro-imaging studies, Mosconi and colleagues [34] used a conventional saccade adaptation test to assess the integrity of the cerebellar network in individuals with ASD. Their main hypothesis was that a slower rate of adaptation in ASD group compared with healthy controls reflected a deficit in the cerebellar vermis. The adaptation test used in this study required that individual refine their movement trajectories over trials to minimize error in the focus of gaze at the completion of saccades. In performing this test, ASD individuals adapted at a slower rate than healthy controls, but they do not show impairment in average accuracy of saccades during baseline, suggesting that cerebellar circuitry supporting online adjustment may be selectively altered.

As well as the rapid eye-movements named saccades, also the slow eye-movements involved in the visual pursuit have been investigated in individuals with ASD.

In fact, the smooth pursuit system is very complex and allows approximating the velocity of a moving target in order to focus the visual image on the fovea. This system is immature at birth and significantly improves during the first year of life [31]. Its integrity in autism was analyzed by Takarae et al. [53], recording the performance of a large sample of highfunctioning individuals with ASD in three types of task. Despite individuals with ASD had normal pursuit latency, they showed a deficit in the initial open-loop stage of pursuit only when targets were moving in the right hemifield and a bilaterally poorer closed-loop pursuit gain. Moreover, pursuit deficits correlated with poorer manual praxis in individuals with ASD. According to these authors, a possible distributed network dysmaturity would be a crucial characteristic of ASD, and they suggest the presence of functional connectivity deficits in the sensorimotor domain and a developmental failure in the sensorimotor systems.

Also, Wilkes and colleagues [57] examined oculomotor behaviors in a group of high-functioning ASD and measured the correlation between oculomotor abnormalities and ASD symptoms. They highlighted abnormal visual smooth pursuit on the vertical plane and a greater latency for initiating saccades in the ASD group and found significant correlations between oculomotor deficit and scores on gold-standard tests for ASD.

#### Visual attention in ASD

The analysis of eye-movements can provide several information about what element of the environment attract the visual attention of an individual. The gaze orienting is driven by both exogenous and endogenous properties: endogenous properties relate to internal states, such as speed of processing, motivation toward the stimuli and vigilance, while the exogenous properties refer to the salience and the physical characteristics of a stimuli [46].

Several hypotheses have been proposed to explain the possible mechanisms underlying the difficulties in visual attention often reported in individuals with ASD since an early age. Unfortunately, results do not always appear homogeneous, and a clear picture of this topic still lacks.

Van Der Geest and collaborators [54] explored the ability to (dis-)engage visual attention through a saccadic gap-overlap paradigm in a group of high-functioning children with ASD. The gap overlap paradigm has been frequently used to analyze the disengagement of attention in individuals with ASD, because it provides two different measures: the gap phase (in which the central fixation point disappears and the peripheral one appears after a 200 ms of temporal gap) provides an indication of the oculomotor efficiency, and the overlap phase (in which the central fixation point remains visible while the peripheral one appears) provides an additional indication of oculomotor efficiency and attentional orienting. In this study, the mean latencies of saccadic eye movements made in the direction of the target were computed for the gap and the overlap conditionseparately. The gap effect was defined as the difference in saccadic latencies between the overlap condition and the gap condition. Van der Geest et al. [53] found a reduced gap effect in the ASD group, meaning that they show smaller difference in the saccadic reaction time between the two conditions. Authors hypothesized that the smaller gap effect was due to a weaker attentional engagement, rather than to a deficit of the attentional disengagement as often reported in literature.

The hypothesis of a failure in the regulation of visual attention, particularly in the fixation and shifting of eye movements, was proposed also by Billeci and colleagues [6], who implemented an eye-tracking paradigm to analyze both responding and initiating joint attention in toddlers with ASD. Joint attention represents the human ability to coordinate the attention with a social partner, with the purpose of sharing the interest about an object or an event; a joint attention act can be performed by following ("response to joint attention (RJA)") or directing ("initiation of joint attention (IJA)") the gaze of a social partner [35]. A joint attention deficit is considered one of the earliest and core symptom of

ASD and it often represents a specific target of the evidencebased early treatments [21]. During their eye-tracking paradigm of joint attention, Billeci et al. [6] described many differences in visual patterns of toddlers with ASD compared with typical developing toddlers. Surprisingly, no differences were found in the responding to joint attention task: ASD toddlers showed a number of gaze-shifting from face to the target objects not significantly different from typical developing toddlers. On the other hand, in the initiating joint attention task, toddlers with ASD showed different pattern of transition and gaze-shifting compared with the controls. Specifically, ASD group looked longer at face and had more gazeshifting from face to the target object, while the control toddlers showed more fixations to the object and more gazeshifting from the object to face. Contrary to the study of Van Der Geest and colleagues cited above, authors suggested that these results could indicate an impairment in the global monitoring of the scene due to difficulties in visual disengagement rather that to difficulties in the gaze following process.

A diminished visual monitoring and visual responsivity to social-cues signaling goal-directedness was the main result of a study conducted by Vivanti et al. [55]. The authors used an eye-tracking paradigm to investigate the ability of a group of ASD children to direct their visual attention toward an agent's face in order to predict imminent action. The findings of this study suggest that difficulties in social understanding and social learning may be due, almost in part, to different patterns of visual attention present in ASD individuals. This idea was also investigated by Groen and colleagues [23] that tried to establish if very young children with ASD might have different perceptual style during the visual scanning of the social environment and whether atypical perceptual styles are present in their parents as well. In this paper, the authors found that the atypical perceptual style during visual exploration of movies is not solely limited to the social domain in the groups of ASD children and that higher ADOS scores (that means higher symptom severity) relates to more abnormal watching behavior. Furthermore, this atypical gaze pattern was present also in the mothers, suggesting that the abnormal visual behavior is crucial into the concept of perceptual broader autism phenotype (BAP). With the term BAP, we refer to a set of subclinical ASD traits that are common in the families of individuals with ASD [48]. These cognitive and personality characteristics are similar to those of individuals with ASD but are milder, even though these represent a risk factor for the development of anxiety disorders, especially during the late toddlerhood or the adolescence period [52].

Chawarska and colleagues [9] investigated the ability to deploy attention based on the perception of eye movement in 2-year-old children with ASD and their chronological age-matched typically developing children. The study involved two experiments with cues consisting of biological and non-biological movements respectively. The authors suggest that the difference between ASD and typical developing children is not absolute but cue specific. In fact, they found that children with autism had significantly shorter saccadic reaction times to peripheral targets as compared with controls when presented an eye-movement cue and both groups had similar and relatively short saccadic reaction times to peripheral targets when the cue consisted of non-biological movement.

In a subsequent study, the same authors [10] extended the results from the previous experiment finding that the cue features affect the regulation of the attentional disengagement. The toddlers with ASD show a faster disengagement from faces, compared with typical developing and developmental delayed toddlers. The same effect was not present in response to non-facial stimuli. The authors suggest that, in children with ASD, the faces have a lower capacity to engage visual attention as pointed out by the shorter time required to disengage attention to fixate on an appearing peripheral target. Hence, ASD children show a reduced availability to conduct an indepth analysis of the characteristics of a novel face, contrary to what happens in typical developing individuals.

Even if the relationship between attention disengagement and depth of processing has not been directly studied in infancy, a large amount of study reports abnormalities in the visual processing in ASD, related to atypical cortical mechanisms. In a recently published study, Murphy and colleagues [36] found difference in the activation of brain regions in response to the presentation of nonsocial stimuli. The result is coherent with the hypothesis of atypical reactions to the salience of the stimuli, suggesting that this can be related to the hyper-sensitivity to visual salience or to the preference for the sameness. Notably, this study does not use social stimuli in order to verify how the attention deficit is specific for this class of stimuli. The findings indicate that atypical neural responses to salient stimuli extend to information without social value.

To disentangle the issue of how visual attention disorder reflects a deficit in basic cortical processes and how much they are influenced by the characteristics of the stimuli is crucial, following this line, McPartland and collaborators [32] examined the influence of the visual properties of static stimuli on a screen, without competitors, on visual attention in adolescents with ASD. The study displayed comparable patterns of visual attention across stimulus categories. Both groups tended to focus attention on the upper regions of the stimuli and paid less attention to the lower regions, particularly for upright face stimuli. Adolescents with ASD exhibited normative patterns of visual attention to human faces despite face recognition impairments and significant social deficits. Hence, the condition "without competitors" might facilitate ASD individuals in properly orienting visual attention, but impaired performance in other conditions might reflect difficulties in deploying attention toward different simultaneous stimuli as, for example, in the case of the scanning of the surrounding environment.

#### Visual-motor integration in children with ASD

The VB is fundamental for the exploration of the surrounding environment and for social learning. On the other hand, it provides the perceptual basis for organizing movement in actions, hence for planning and for guiding the movement toward a goal. According to this idea, action is a necessary part itself of the perceptual process and appears crucial for the human being's adaptation [24]. Several authors described different degrees of impairment of the VB and motor functions integration in individuals with ASD [14, 18, 33]. These findings have been also reported in f-MRI studies, in which an increased visual-motor temporal incongruity was found in ASD children rather than in TD children [37]. Moreover, Nebel and collaborators [37] reported a relationship between the ability to combine gestures and visual-motor connectivity in children with ASD.

This correlation may also represent a possible association to motor learning data, since, in ASD population, motor coordination disorders have been already observed during the early infancy; infact, gross motor delay, fine motor dysfunctions, postural control difficulties, imitation deficits, and praxis impairments have been broad reported in scientific literature [5].

Miller and colleagues [33] explored specifically the presence of an ideational dyspraxia and its association with different underlying motor functions, including oculomotor function and visual-motor integration. Ideational dyspraxia tasks used in this study consist of a sequence of actions that subject were required to perform in a prescribed order. Children with poor motor timing performed worse on all praxis tasks and had slower and less accurate eye movements while those with regular timing performed as well as typical children on those same tasks. They suggested that ideational dyspraxia in ASD could involve cerebellar mechanisms of movement control, given that the integration of these mechanisms with cortical networks is involved in praxis.

Sharer and collaborators [51] assessed neural activity patterns and sequence learning differences in a group of children with ASD, during a serial reaction time task adapted for the administration of a f-MRI paradigm. Authors reported significant differences in neural recruitment during visual-motor learning task, particularly within the initial stages of the learning process. Mainly, children with ASD demonstrated reduced activity, as compared with typical peers, in the superior temporal sulcus and posterior cingulate cortex, regions known to be important in visual-motor control and in the sequence learning.

In the attempt to better understand how integration of visual information affect learning of social actions, Sharer et al. [50] used a modified serial reaction time task to explore the use of visual information in promoting motor learning in a group of adults with ASD. Participants were trained using their dominant hand and tested using their untrained hand. The results showed that ASD participants do not utilize extrinsic-visual aspect from training to generalize the learned sequence to the untrained hand, suggesting that ASD individuals under-utilize visual input during motor learning.

Because of the importance of the VB in the motor learning, visual-motor difficulties reported during infancy of ASD individuals might impact the overall adaptive postural-motor development. As a matter of fact, a generalized motor control difficulty in children with ASD (such as in manual dexterity, in aiming and catching skills, and in balance abilities) mainly in the dynamic and unpredictable environment, correlates with a greater intensity and frequency of repetitive behaviors (particularly ritualistic behavior) (Giulia [43]). It is possible that, as suggested by Radonovich and collaborators [44] a delayed or abnormal postural control may, in turn, constrain the ability of children of visual exploration of the surrounding environments.

The dysfunction in the use of visual information for the online control of the motion trajectory, and for the selection of a motor program appropriate to plan an action or a sequence of actions, seems to have its base on an increased "dorsal stream vulnerability", as focused by Braddick and Atkinson [7]. The dorsal pathway plays an important role in feeding specific visuomotor modules for the control of actions, and in managing visual behavior through spatially directed attention in the environment. A dysfunction of the visual dorsal stream is reported in various neurodevelopmental disorders, including ASD [3, 7, 8].

# Implication for early diagnosis and intervention in ASD

This brief review aims to furnish insights about the question if VB abnormalities may have a role in the onset of ASD and, if yes, through which mechanism. Our hypothesis is that visual behavior abnormalities may affect experiences that infants carry on during the first steps of life by using visual modalities of social world perception.

Taken together, these studies support the need for a deep investigation on visual behaviors impairments, in order to figure out the debatable issue of the role played by the failure to develop normal visual functions in the social impairments in ASD. Even if these behaviors are not usually investigated, because they are not considered core symptoms of ASD, they potentially could have cascading effects on the overall development and, for these reasons, could be considered as prodromal signs of the disorder. For example, the presence of a failure in the development of visual behaviors may affect infant's ability to correctly use the gaze in the exploration of their environment and in the processing of the surrounding social and non-social stimuli. In addition, several studies reported that perceptual and motor impairments are evident before the onset of social impairments [13, 16, 19, 42], suggesting an early disruption of mechanisms devoted to organize and control movement for social purpose. These findings might suggest that, for example, the atypical eye contact could be the clearer and more explicit symptom of a visual-perceptual impairment intrinsic to the neurobiological disorder of ASD.

Several components of VB could be early detected by clinicians. For example, eye-tracking methodology can be further implemented to analyze disruptions in visual orienting mechanisms that have been proved to be altered in very young infants at risk who subsequently received a diagnosis of ASD: in fact, Elison et al. [15] found that 7-month old who went on to develop ASD, showed a delayed disengagement of visual attention when viewing social and non-social stimuli during a gap-overlap paradigm. The eye-tracking could be considered a valid methodology to support clinical practice, especially during the assessment of visual orienting mechanisms, and might help to detect behaviors and subtle atypical signs that are difficult to be detected otherwise, and allows a reliably assessment in early infancy [1].

In addition, given that the VB is the first channel to communicate with others, the clinical evaluation of early visual functions through appropriate, low-cost, and non-invasive tools for infants and children is considered an important part of the clinical practice in the follow-up of children at risk for neurodevelopmental disorders. In fact for a few years, several standardized protocols have been developed for use from clinicians to assess oculomotor abilities, visual acuity and stereopsis, visual attention, and visual field in very young infants [41, 45, 47].

Hence, the investigation of VB might be also considered a critical target in the early identification processes. Their assessment is simple, not invasive, and based on objective methodology. In fact, if an early deficit in the domain of visual behavior will be further identified as a prodromal sign of a neurodevelogerdpmental disorder, this might also be considered for the development of tailored treatments. To date, an early diagnosis, followed by an early intensive treatment, is pivotal to improving the outcomes of children diagnosed with ASD, especially when the intervention is based on the developmental profile of the child [12]. Even if the domain of visual behaviors is not considered yet in the context of early treatment of ASD, some authors reported successful training programs based, for example, on the oculomotor deficit or on the visual attentional control in infancy [56]. In conclusion, since the key-role of VB for navigating and for orienting visual attention to spatial locations containing pertinent information for adaption, a clear description of this deficit in the context of an early diagnosis, could help to identify clinical subgroups, in which visual perceptual difficulties in children with ASD are present to a more or a less extent [17, 57] and might improve the development of more personalized treatments.

Authors' Contributions FA had the primary responsibility for the analysis of literature and for writing the manuscript. VC participated in the development of the theoretical framework and contributed to the writing of the manuscript. GP was responsible for the idea of this mini review, supervised the design and execution of the review and contributed to the writing of the manuscript for the final version. All authors reviewed the final manuscript.

## **Compliance with ethical statements**

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

# References

- Alahyane N, Lemoine-Lardennois C, Tailhefer C, Collins T, Fagard J, Doré-Mazars K (2016) Development and learning of saccadic eye movements in 7- to 42-month-old children. J Vis 16(1):6. https://doi.org/10.1167/16.1.6
- American Pychiatric Association (2013) Diagnostic and statistical manual of mental disorders: DSM-5<sup>TM</sup>, 5th ed. Arlington, VA, US: American Psychiatric Publishing, Inc https://doi.org/10.1176/appi. books.9780890425596
- Atkinson J (2017) The davida teller award lecture, 2016 visual brain development: a review of "dorsal stream vulnerability"-motion, mathematics, amblyopia, actions, and attention. J Vis 17(3):1–24. https://doi.org/10.1167/17.3.26
- 4. Baio J, Wiggins L, Christensen DL, Maenner MJ, Daniels J, Warren Z, Kurzius-Spencer M, Zahorodny W, Robinson Rosenberg C, White T, Durkin MS, Imm P, Nikolaou L, Yeargin-Allsopp M, Lee LC, Harrington R, Lopez M, Fitzgerald RT, Hewitt A, Pettygrove S, Constantino JN, Vehorn A, Shenouda J, Hall-Lande J, van Naarden Braun K, Dowling NF (2018) Prevalence of autism spectrum disorder among children aged 8 years autism and developmental disabilities monitoring network, 11 sites, United States, 2014. MMWR Surveill Summ 67(6):1–23. https://doi.org/10.15585/mmwr.ss6706a1
- Bhat AN, Landa RJ, Galloway JC(C) (2011) Current perspectives on motor functioning in infants, children, and adults with autism spectrum disorders. Phys Ther 91(7):1116–1129. https://doi.org/10. 2522/ptj.20100294
- Billeci L, Narzisi A, Campatelli G, Crifaci G, Calderoni S, Gagliano A et al (2016) Disentangling the initiation from the response in joint attention: an eye-tracking study in toddlers with autism spectrum disorders. Transl Psychiatry 6(5). https://doi.org/ 10.1038/tp.2016.75
- Braddick O, Atkinson J (2011) Development of human visual function. Vis Res 51(13):1588–1609. https://doi.org/10.1016/j.visres. 2011.02.018
- Braddick O, Atkinson J (2013) Visual control of manual actions: brain mechanisms in typical development and developmental disorders. Dev Med Child Neurol 55(SUPPL.4):13–18. https://doi. org/10.1111/dmcn.12300

- Chawarska K, Klin A, Volkmar F (2003) Automatic attention cueing through eye movement in 2-year-old children with autism, 74(4), 1108–1122
- Chawarska K, Volkmar F, Klin A (2010) Limited attentional bias for faces in toddlers with autism spectrum disorders. Arch Gen Psychiatry 67(2):178–185. https://doi.org/10.1001/ archgenpsychiatry.2009.194
- Cheung CHM, Bedford R, Johnson MH, Charman T, Gliga T (2018) Visual search performance in infants associates with later ASD diagnosis. Dev Cogn Neurosci 29:4–10. https://doi.org/10. 1016/J.DCN.2016.09.003
- Dawson G, Rogers S, Munson J, Smith M, Winter J, Greenson J, Donaldson A, Varley J (2010) Randomized, controlled trial of an intervention for toddlers with autism: the early start Denver model. Pediatrics 125(1):e17–e23. https://doi.org/10.1542/peds.2009-0958
- Di Giorgio E, Frasnelli E, Rosa Salva O, Maria Luisa S, Puopolo M, Tosoni D et al (2016) Difference in visual social predispositions between newborns at low-and high-risk for autism. Sci Rep 6:1– 8. https://doi.org/10.1038/srep26395
- Dowd AM, McGinley JL, Taffe JR, Rinehart NJ (2012) Do planning and visual integration difficulties underpin motor dysfunction in autism? A kinematic study of young children with autism. J Autism Dev Disord 42(8):1539–1548. https://doi.org/10.1007/ s10803-011-1385-8
- Elison JT, Paterson SJ, Wolff JJ, Reznick JS, Sasson NJ, Gu H et al (2013) White matter microstructure and atypical visual orienting in 7-month-olds at risk for autism. Am J Psychiatr 170(8):899–908. https://doi.org/10.1176/appi.ajp.2012.12091150
- Esposito G, Venuti P, Maestro S, Muratori F (2009) An exploration of symmetry in early autism spectrum disorders: analysis of lying. Brain and Development 31(2):131–138. https://doi.org/10.1016/J. BRAINDEV.2008.04.005
- Freedman EG, Foxe JJ (2018) Eye movements, sensorimotor adaptation and cerebellar-dependent learning in autism: toward potential biomarkers and subphenotypes. Eur J Neurosci 47(6):549–555. https://doi.org/10.1111/ejn.13625
- Glazebrook C, Gonzalez D, Hansen S, Elliott D (2009) The role of vision for online control of manual aiming movements in persons with autism spectrum disorders. Autism 13(4):411–433. https://doi. org/10.1177/1362361309105659
- Gliga T, Bedford R, Charman T, Johnson MH, Baron-Cohen S, Bolton P et al (2015) Enhanced visual search in infancy predicts emerging autism symptoms. Curr Biol 25(13):1727–1730. https:// doi.org/10.1016/J.CUB.2015.05.011
- Goldberg MC, Lasker AG, Zee DS, Garth E, Tien A, Landa RJ (2002) Deficits in the initiation of eye movements in the absence of a visual target in adolescents with high functioning autism, 40, 2039–2049
- Goods KS, Ishijima E, Chang Y-C, Kasari C (2013) Preschool based JASPER intervention in minimally verbal children with autism: pilot RCT. J Autism Dev Disord 43(5):1050–1056. https://doi. org/10.1007/s10803-012-1644-3
- Grice SJ, Halit H, Farroni T, Baron-Cohen S, Bolton P, Johnson MH (2005) Neural correlates of eye-gaze detection in young children with autism. Cortex 41(3):342–353. https://doi.org/10.1016/ S0010-9452(08)70271-5
- Groen WB, Rommelse N, de Wit T, Zwiers MP, van Meerendonck D, van der Gaag RJ, Buitelaar JK (2012) Visual scanning in very young children with autism and their unaffected parents. Autism Res Treat 2012:1–9. https://doi.org/10.1155/2012/748467
- Von Hofsten C (2009) Action, the foundation for cognitive development. Scand J Psychol 50(6):617–623. https://doi.org/10.1111/j. 1467-9450.2009.00780.x
- Jones EJH, Gliga T, Bedford R, Charman T, Johnson MH (2014) Developmental pathways to autism: a review of prospective studies

of infants at risk. Neurosci Biobehav Rev 39:1–33. https://doi.org/ 10.1016/J.NEUBIOREV.2013.12.001

- Kemner C, Verbaten MN, Camfferman JMCG, Engeland H Van. (1998) Abnormal saccadic eye movements in autistic children, 28(I)
- Land MF (2009) Vision, eye movements, and natural behavior, 51–62. https://doi.org/10.1017/S0952523808080899
- Lord C, Rutter M, DiLavore PC, Risi S, Gotham K, Bishop S (2012a )Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) Manual (Part I): Modules 1–4. Torrance, CA: Western Psychological Services
- Lord C, Luyster R, Gotham K, Guthrie W (2012b) Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) Manual (Part II): Toddler Module. Torrance, CA: Western Psychological Services
- 30. Zwaigenbaum L, Bauman ML, Stone WL, Yirmiya N, Estes A, Hansen RL, McPartland JC, Natowicz MR, Choueiri R, Fein D, Kasari C, Pierce K, Buie T, Carter A, Davis PA, Granpeesheh D, Mailloux Z, Newschaffer C, Robins D, Roley SS, Wagner S, Wetherby A (2019) Early identification of autism spectrum disorder: recommendations for practice and research abstract. Pediatrics 136:S10–S40
- Luna B, Velanova K, Geier CF (2009) Development of eyemovement control, 68(3), 293–308. https://doi.org/10.1016/j. bandc.2008.08.019.Development
- Mcpartland JC, Webb SJ, Keehn B (2011) Spectrum disorder, 41(2), 148–157. https://doi.org/10.1007/s10803-010-1033-8. Patterns
- Miller M, Chukoskie L, Zinni M, Townsend J, Trauner D (2014) Dyspraxia, motor function and visual–motor integration in autism. Behav Brain Res 269:95–102. https://doi.org/10.1016/J.BBR.2014. 04.011
- Mosconi MW, Luna B, Kay-stacey M, Nowinski CV, Rubin LH, Scudder C, ... Sweeney JA (2013) Saccade adaptation abnormalities implicate dysfunction of cerebellar-dependent learning mechanisms in autism spectrum disorders (ASD), 8(5). https://doi.org/10. 1371/journal.pone.0063709
- Mundy P, Jarrold W (2010) Infant joint attention, neural networks and social cognition. Neural Netw 23(8–9):985–997. https://doi. org/10.1016/j.neunet.2010.08.009
- Murphy ER, Norr M, Strang JF, Kenworthy L, Gaillard WD, Vaidya CJ (2017) Neural basis of visual attentional orienting in childhood autism spectrum disorders. J Autism Dev Disord 47(1): 58–67. https://doi.org/10.1007/s10803-016-2928-9
- Nebel MB, Eloyan A, Nettles CA, Sweeney KL, Ament K, Ward RE, Choe AS, Barber AD, Pekar JJ, Mostofsky SH (2016) Intrinsic visual-motor synchrony correlates with social deficits in autism. Biol Psychiatry 79(8):633–641. https://doi.org/10.1016/j.biopsych. 2015.08.029
- Nichols CM, Ibañez LV, Foss-Feig JH, Stone WL (2014) Social smiling and its components in high-risk infant siblings without later ASD symptomatology. J Autism Dev Disord 44(4):894–902. https://doi.org/10.1007/s10803-013-1944-2
- Pensiero S, Fabbro F, Michieletto P, Accardo A, Brambilla P (2009) Saccadic characteristics in autistic children. Funct Neurol 24(3): 153–158 Retrieved from https://www.functionalneurology.com/ materiale\_cic/440\_XXIV\_3/3882\_saccadic/index.html
- Port NL, Trimberger J, Hitzeman S, Redick B, Beckerman S (2016) Micro and regular saccades across the lifespan during a visual search of "Where's Waldo" puzzles. Vis Res 118:144–157. https:// doi.org/10.1016/J.VISRES.2015.05.013
- Purpura G, Bacci GM, Bargagna S, Cioni G, Caputo R, Tinelli F (2019) Visual assessment in down syndrome: the relevance of early visual functions. Early Hum Dev, 131. https://doi.org/10.1016/j. earlhumdev.2019.01.020

- Purpura G, Costanzo V, Chericoni N, Puopolo M, Scattoni ML, Muratori F, Apicella F (2017) Bilateral patterns of repetitive movements in 6- to 12-month-old infants with autism spectrum disorders. Front Psychol, 8(JUL). https://doi.org/10.3389/fpsyg.2017.01168
- Purpura G, Fulceri F, Puglisi V, Masoni P, Contaldo A (2016) Motor coordination impairment in children with autism spectrum disorder: a pilot study using movement assessment battery for Children-2 checklist - Minerva Pediatrica 2016 Oct 12 - Minerva Medica journals. Minerva Pediatr, Oct 12. Retrieved from https://www. minervamedica.it/en/journals/minerva-pediatrica/article.php?cod= R15Y9999N00A16101202
- Radonovich KJ, Fournier KA, Hass CJ (2013) Relationship between postural control and restricted, repetitive behaviors in autism spectrum disorders. Front Integr Neurosci 7:28. https://doi.org/10. 3389/fnint.2013.00028
- 45. Ricci D, Romeo DM, Gallini F, Groppo M, Cesarini L, Pisoni S, Serrao F, Papacci P, Contaldo I, Perrino F, Brogna C, Bianco F, Baranello G, Sacco A, Quintiliani M, Ometto A, Cilauro S, Mosca F, Romagnoli C, Romeo MG, Cowan F, Cioni G, Ramenghi L, Mercuri E (2011) Early human development early visual assessment in preterm infants with and without brain lesions: correlation with visual and neurodevelopmental outcome at 12 months. Early Hum Dev 87(3):177–182. https://doi.org/10.1016/j. earlhumdev.2010.12.003
- Richards JE, Reynolds GD, Courage ML (2010) The neural bases of infant attention. Curr Dir Psychol Sci 19(1):41–46. https://doi. org/10.1177/0963721409360003
- Rowe FJ, Hepworth LR, Hanna KL, Howard C (2018) Visual impairment screening assessment (VISA) tool: pilot validation. BMJ Open 8(3):e020562. https://doi.org/10.1136/bmjopen-2017-020562
- Rubenstein E, Chawla D (2018) Broader autism phenotype in parents of children with autism: a systematic review of percentage estimates. J Child Fam Stud 27(6):1705–1720. https://doi.org/10. 1007/s10826-018-1026-3
- Salman MS, Sharpe JA, Eizenman M, Lillakas L, Westall C, To T et al (2006) Saccades in children, vol 46, pp 1432–1439. https://doi. org/10.1016/j.visres.2005.06.011

- Sharer EA, Mostofsky SH, Pascual-Leone A, Oberman LM (2016) Isolating visual and proprioceptive components of motor sequence learning in ASD. Autism Res 9(5):563–569. https://doi.org/10. 1002/aur.1537
- Sharer E, Crocetti D, Muschelli J, Barber AD, Nebel MB, Caffo BS, Pekar JJ, Mostofsky SH (2015) Neural correlates of visuomotor learning in autism. J Child Neurol 30(14):1877–1886. https://doi. org/10.1177/0883073815600869
- 52. Shephard E, Milosavljevic B, Pasco G, Jones EJH, Gliga T, Happé F et al (2017) Mid-childhood outcomes of infant siblings at familial high-risk of autism spectrum disorder. Autism Res 10(3):546–557. https://doi.org/10.1002/aur.1733
- Takarae Y, Minshew NJ, Luna B, Krisky CM, Sweeney JA (2004) Pursuit eye movement deficits in autism, 2584–2594. https://doi. org/10.1093/brain/awh307
- Van der Geest JN, Kemner C, Camfferman G, Verbaten MN, Van Engeland H (2001) Eye movements, visual attention, and autism: a saccadic reaction time study using the gap and overlap paradigm. Biol Psychiatry 50(8):614–619. https://doi.org/10.1016/S0006-3223(01)01070-8
- Vivanti G, Trembath D, Dissanayake C (2014) Atypical monitoring and responsiveness to goal-directed gaze in autism spectrum disorder. Exp Brain Res 232(2):695–701. https://doi.org/10.1007/ s00221-013-3777-9
- Wass S, Porayska-Pomsta K, Johnson MH (2011) Training attentional control in infancy. Curr Biol 21(18):1543–1547. https://doi. org/10.1016/J.CUB.2011.08.004
- Wilkes BJ, Carson TB, Patel KP, Lewis MH, White KD (2015) Oculomotor performance in children with high-functioning autism spectrum disorders. Res Dev Disabil 38:338–344. https://doi.org/ 10.1016/J.RIDD.2014.12.022

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.