Received: 28 November 2022 | Revised: 17 March 2023 | Accepted: 3 May 2023

DOI: 10.1002/jdn.10276

RESEARCH ARTICLE

INTERNATIONAL JOURNAL OF DEVELOPMENTAL NEUROSCIENCE

ISDN WILEY

Inhibition functions can be improved in children with autism spectrum disorders: An eye-tracking study

Simona Caldani[1,2] | Elise Humeau[3,4,5] | Richard Delorme[3,4,5] | Maria Pia Bucci[1,2]

[1]MoDyCo, UMR 7114 CNRS, Paris Nanterre University, Nanterre, France

[2]EFEE–Center for the Functional Exploration of Balance in Children, Robert Debré Hospital, Paris, France

[3]Child and Adolescent Psychiatry Department, Robert Debré Hospital, Paris, France

[4]High Functioning Autism Expert Centre, Fundamental Fondation, Paris, France

[5]Paris University, Paris, France

Correspondence
Maria Pia Bucci, UMR 7114 MoDyCo, CNRS Paris University, 92001 Nanterre, France.
Email: mariapia.bucci@gmail.com

Abstract

Cognitive remediation therapy interventions could improve cognitive functioning in subjects with autism. To investigate the benefit of a short cognitive training rehabilitation in children with autism spectrum disorder (ASD) on pursuit and fixation performances. We recruited two groups (G1 and G2) of 30 children with ASD, sex-, IQ- and age-matched (mean 11.6 ± 0.5 years), and pursuit and fixation eye movements were recorded twice at T1 and T2. Between T1 and T2, a 10-min cognitive training was performed by the G1 group only, whereas the G2 group had a 10-min of rest. For all children with ASD enrolled in the study, there was a positive correlation between restricted and repetitive behaviour scores of both Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS) and the number of saccades recorded during the fixation task at T1. At T1, oculomotor performances were similar for both groups of ASD children (G1 and G2). At T2, we observed a significant reduction in the number of saccades made during both pursuit and fixation tasks. Our findings underlined the importance to promote cognitive training rehabilitation for children with ASD, leading to a better performance in inhibitory and attention functioning responsible for pursuit and fixation eye movement's performance.

KEYWORDS

autism spectrum disorder, children, eye movements, inhibitory mechanism

1 | INTRODUCTION

Autism spectrum disorders (ASDs) correspond to neurodevelopmental disorders characterized by social communication and social interaction deficits, associated with the presence of restricted, repetitive and stereotyped behaviours (DSM-5, American Psychiatric Association APA, 2013). Numerous neuroimaging studies in ASD reported atypical brain functioning, for instance, lower levels of synchronization between the inhibition network (anterior cingulate gyrus, middle cingulate gyrus and insula) and the right middle and inferior frontal and right inferior parietal regions (Pereira et al., 2018), or lower levels of functional connectivity and less network integration between frontal, parietal and occipital regions (Ha et al., 2015). Note

Abbreviation: ANOVA, Analysis of variance.

that, all these brain regions are responsible for cognitive activities, particularly executive functions including attention, processing information or inhibitory control (Fiske & Holmboe, 2019).

Inhibitory control is considered a key executive control process that helps govern complex cognition and in turn complex adaptive behaviour; moreover, it involves preparing for responding, monitoring performance and detecting errors (Tiego et al., 2018).

In literature, several studies reported reduced behavioural inhibition and low resistance to distractors in subjects with ASD (see Geurts et al., 2014, for meta-analysis). Indeed, these authors in a large number of studies reported a medium effect size for behavioural inhibition and a small effect for low resistance to distractors, with age moderating the effect of behavioural inhibition and intelligence quotient (IQ) moderating low resistance to distractors. They suggested that subjects with ASD are characterized by inhibition impairment; particularly, they showed important difficulties to inhibit prepotent behavioural responses, whereas their ability to inhibit attention towards distractors is less affected. Moreover, Geurts and collaborators underlined the multi-faceted nature of inhibition showing its relationship with factors such as age and IQ.

However, in the literature, discrepant findings on this issue have been reported. Van den Bergh et al. (2014), for example, tested in 102 school-aged children with ASD the relationship between inhibitory control system and the intensity of autistic symptoms (such as restricted, repetitive and stereotyped behaviours, interests and sensorimotor behaviours), and they suggested that inhibition processes were related only to higher intensity of these symptoms. Schmitt et al. (2018) reported in a large sample of subjects with ASD from 5 to 28 years old that the presence of inhibitory control deficits was linked more to a reduced ability to delay the onset of the responses rather than to stop inappropriate responses.

Over the past decades, eye movements have increasingly been applied as an experimental tool to gain objective insight into cognitive deficits given that studying eye movement control allows to understand how the brain is working. Indeed numerous ingenious paradigms have been developed to describe their underlying neurological and cognitive substrates for better comprehension of neurodevelopmental disorders (Rommelse et al., 2008).

Indeed, eye movement's recordings have been frequently used to explore brain activities in subjects with ASD and could represent objective and quantitative biomarkers of cortical network dysfunctions in these patients. In laboratory, different types of paradigms can be used to test attention and inhibitory capabilities, for instance, pursuit's eye movements and fixations. In fact, pursuits allow the eyes to track a moving object keeping it close to the fovea, and fixation is needed to maintain the image of interest on the fovea. Both tasks involve attention and inhibitory control mechanisms, which are controlled by frontal eye field activity (Izawa & Suzuki, 2014).

In the literature, deficits in pursuit and fixation performances have been documented in subjects with autism. For instance, Takarae et al. (2004) reported in a large group of subjects with autism (from 8 to 53 years old) poor gain when pursuits were elicited with constant velocity as well as oscillating target most likely because of sensorimotor deficiencies and deficits in generating predictive responses. Interestingly, this deficit was more important after mid-adolescence, suggesting a delayed maturation of cortical structures triggering pursuit's eye movements in subjects with autism. Later on, the same group of researchers (Takarae et al., 2007) suggested that subjects with ASD could have lower levels of activity in cortical areas, such as frontal eye fields, parietal cortex and dorsolateral prefrontal cortex, which have been responsible for cognitive capabilities as anticipation, inhibition and attention related to eye movement performance.

Several studies tested eventual benefit of cognitive and/or attentional training types in subjects with ASD. For instance, Chukoskie et al. (2018) tested a new training tool in order to improve attention capabilities in children with ASD, and they showed that after video-game exercises (30 min, five times per week for 8 weeks), children with ASD improved significantly attention capabilities and gaze that are skills used in social communication and in other cognitive functions. In line with this thinking, Pastor-Cerezuela et al. (2020) reported that in children with ASD, sensory and cognitive dysfunctions are in relationship with executive deficits and inhibitory control.

Dandil et al. (2020) made a review on how cognitive remediation therapy interventions can improve cognitive functioning in subjects with autism. These types of training were usually done for a long period; for instance, Eack et al. (2018) reported that an 18-month neurocognitive and social–cognitive remediation in adult subjects with ASD significantly improved mental activities and attention capabilities. Recently, Hajri et al. (2022) in a perspective paper type highlighted the importance of developing cognitive re-education in subjects with ASD in order to improve several daily life activities related to executives functions such as inhibition, working memory and attention; most importantly, they suggested that such re-education needs to be done as early as possible in these kinds of subjects. In line with this thinking, Miranda et al. (2017) explored the relationship between executive functions and social cognition in subjects with ASD, and they showed a strong association between social cognition and cognitive abilities such as initiation and planning. Vogan et al. (2018) examining executive functions in children with ASD reported that executive functions are predictive of later social, emotional and behavioural problems in children with ASD. These authors suggested that executive functions could be considered as a potential target of intervention for preventing and reducing psychopathology and promoting social competence in children with ASD.

To our knowledge, few studies explored how different executive function interventions could improve flexibility and inhibitory capabilities in subjects with ASD. For instance, Stichter and colleagues (2010) examined the effectiveness of a social competence intervention on 27 students with ASD aged from 11 to 14 years old. They used the Social Competence Intervention (SCI) program that is focused on training social communication skills including turn-taking, recognizing feelings and facial expressions in others and problem solving. This program consists of five units (each composed of 4- to 1-h lessons) over 2 weeks. These authors reported improvements in the theory of mind that corresponds to the capacity to understand other people by ascribing mental states of them, as well as problem-solving abilities. Interestingly, they reported also improvements concerning executive functions (assessed only subjectively) following parent reports. Note that the presence of deficits in executive functioning could have an impact on the everyday social functioning (Fiefer & Rattan, 2007) and it would seem that explaining the reasoning underlying social competences can improve not only these latter capabilities but also global executive functioning (Ozonoff et al., 1991). Kenworthy et al. (2014) tested in a large number of children with ASD the effect of executive functions intervention, named Unstuck and On Target, for training flexibility, goal-setting and planning abilities. This training type was based on cognitive–behavioural programs. This training consists of 28 lessons lasting 30–40 min each. These authors reported that following this intervention, children with ASD showed a global cognitive improvement in problem solving, flexibility and planning/organizing. They suggested the importance to implement executive functions intervention in educational settings. Morgan et al. (2018) also in order to study the effect of a teacher-implemented, classroom-based Social, Communication, Emotional Regulation, and Transactional Support (SCERTS) intervention on the executive functions and social outcomes recruited 118 children with ASD (mean age = 6.82 years) for 25 h per week and tested the effects of this training. These authors found that SCERTS intervention permits to improve not only social skills but also executive functions in children with ASD and suggested the importance to implement this kind of intervention in the school environment.

TABLE 1 Clinical characteristics of the two groups (G1 and G2) of children with autism spectrum disorder (ASD) enrolled in the study.

	G1 *N* = 30	G2 *N* = 30
Age (years), mean (SD)	11.6 (2.8)	11.5 (2.9)
Diagnosis of ASD		
Autism Diagnostic Interview-Revised scores		
Social reciprocal interaction, mean (SD)	14.8 (6.1)	14.9 (4.9)
Communication, mean (SD)	10.1 (4.2)	10.0 (5.2)
Stereotyped patterns of behaviours, mean (SD)	5.6 (2.3)	5.7 (2.4)
Autism Diagnostic Observation Schedule scores		
Social reciprocal interaction, mean (SD)	10.2 (3.8)	10.5 (2.8)
Communication, mean (SD)	2.9 (1.4)	2.7 (1.5)
Cognitive assessment		
WISC-IV sub-test scores		
Verbal comprehension, mean (SD)	95.9 (25.8)	96.5 (23.2)
Perceptual reasoning, mean (SD)	94.2 (24.1)	92.2 (21.0)
Working memory, mean (SD)	92.5 (20.1)	90.1 (23.1)
Processing speed, mean (SD)	91.2 (18.9)	90.3 (19.0)

In a more recent study, Bremer et al. (2020) reported that physical exercise improved cerebral oxygenation and inhibitory control in a small group of children with ASD, supporting the 'pre-activation' theory (suggested by Budde et al., 2008, and Schmidt et al., 2016), according to which the cognitive engagement of the physical activity actives the same cognitive processes needed for cognitive tasks, like inhibitory control, flexibility, planning or attention.

Based on all this knowledge, we wonder to investigate the benefit of a short rehabilitation cognitive training in children with ASD on oculomotor tasks (pursuits and fixation eye movements). Recall that these types of eye movements need cognitive abilities and they are poorly performed in subjects with ASD (Rommelse et al., 2008).

Our driven hypothesis is that these types of eye movements need to employ executive functions, particularly attention and inhibitory skills that are altered in children with ASD; consequently, these children could benefit from such training. Importantly, we have to point out that, in contrast to other studies in which the improvements have been only subjectively evaluated (by using neuropsychological tests or parent's interviews), oculomotor recordings can objectively assess eventual changes in cognitive abilities. The second objective of this study was to explore whether clinical symptoms in ASD, for instance, the presence of restrictive and repetitive behaviours (RRBs), would be related to the performance of pursuit and fixation eye movements. Given that RRBs interfere with the individual's ability to engage in other activities (e.g., academics or leisure) with a negative impact on social relationships and cognitive abilities, we hypothesized that RRBs could be related to oculomotor performance. Indeed, the connection dysfunction of the cerebellum could be at the origin of both sensorimotor processing and motor control and also RRBs (Tian et al., 2022).

2 | MATERIALS AND METHODS

2.1 | Subjects

Two groups (G1 and G2) of 30 children with ASD, age-, sex- and IQ-matched were included in the study (see Table 1). Children were included at the paediatric university hospital and underwent a neurological exam. None of them reported any personal history of sensory deficit (in any of the five senses), and they were naïve to any psychotropic drugs. The best-estimated diagnosis of ASD was based on DSM-5 criteria requiring to gather clinical information from the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R) associated with the clinical expertise. Their cognitive abilities were also assessed using the Wechsler Intelligence Scale for Children (WISC-IV). The allocation of a child to a specific group (G1 or G2) was generated in an unpredictable random sequence, and the sequence was implemented in a way that concealed the treatments (rest vs. rehabilitation) until children have been formally assigned to one of the two groups.

The investigation followed the principles of the Declaration of Helsinki and was approved by our Institutional Human Experimentation Committee (Comité de Protection des Personnes CPP). Written consents were obtained from the children's parents after the experimental procedure was explained to them.

2.2 | Oculomotor paradigms

Stimulus was presented on a 22″ PC screen with a resolution of 1920 × 1080 and with a refresh rate of 60 Hz. Pursuits and fixations (simple and with distractors) were presented randomly to each child.

2.2.1 | Pursuit

A red circular target (0.5° of visual angle) was moving at a velocity of 15°/s on the PC's screen. The target was initially placed in the central position and then moved horizontally to one side until it reached the ±20° location, where it reversed abruptly and moved to the opposite side. A total of nine trials were run and included in the analysis. A child was instructed to keep his eyes on the target, wherever it moved. After a short break, the child had to perform the same test again (Lions et al., 2013).

In the *simple fixation*, the child was invited to fixate on the target appearing in the centre (filled white circle subtending a visual angle of 0.5°) of the black screen for 30 s. In the second one, named *fixation with distractors*, the child had to maintain fixation on the central target and to inhibit saccades towards the distractors. The distractor was a white smile target (of 0.5°) appearing for a random duration from 500 to 2000 ms and calling for horizontal saccade amplitudes from 5° to 20° (see Caldani et al., 2019). The distractor was presented during the *fixation with distractor* trial (30 s); in total, eight distractors were presented during each *fixation with distractor* trial. Instructions were given to the child to try to fixate on the central target as better as possible (in the *simple fixation* task) and to try to fixate on the central target as better as possible without looking at the distractors (in the *fixation with distractor* task).

2.3 | Eye movement recordings

Eye movements were recorded using an eye tracker (Mobile EBT®, SuriCog), a CE-marked medical eye-tracking device. The Mobile EBT® benefited from cameras that can capture the movements of each eye independently. Recording frequency was set up to 300 Hz. The precision of this system was typically 0.25° (see www.suricog.com, for more details). There was no obstruction of the visual field with this recording system.

2.4 | Procedure

Each child was seated in a chair in a dark room, their head stabilized by a headrest supporting both the forehead and the chin. Viewing was binocular; the viewing distance was 60 cm. Calibration was done at the beginning of each task. During the calibration procedure, children fixated a grid of 13 points (diameter 0.5 deg) mapping the screen. Each calibration point required a fixation of 250 ms to be validated. A polynomial function with five parameters was used to fit the calibration data

INTERNATIONAL JOURNAL OF DEVELOPMENTAL NEUROSCIENCE

and to determine the visual angles. After the calibration procedure, an oculomotor task was presented to the child. The type of task (pursuit, fixation simple or with distractor) was randomly assigned. Each task was kept short (lasting a couple of minutes) to avoid a shift of the helmet and/or head movements of the child, but allowing for an accurate evaluation of eye movement recordings. These measures were done two times, T1 and T2, respectively before and after 10 min of rehabilitation cognitive training for the subjects allocated to group G1, and before and after 10 min of rest (i.e., without any training) for group G2.

2.5 | Rehabilitation cognitive training protocol

After the first oculomotor recording (T1), children with ASD from G1 were trained for cognitive rehabilitation (Figure 1). This training consists of an oculomotor task (memory-guided saccades) for 2 min and a revised Stroop test (several exercises lasting 8 min). Concerning memory-guided tasks, children had to fixate on the central fixation target in the middle of the PC's screen (see Caldani et al., 2022). After the fixation period, a stimulus appeared for 300 ms on the right or the left side of the screen at 20 degrees of eccentricity. The central fixation target extinction occurred 1000 ms after peripheral stimulus presentation. Children were instructed to look at the central fixation target while a peripheral stimulus was switched on, and they had to remember the location of this peripheral stimulus, wait for the extinction of the central fixation target and, only after the fixation target was switched off, make a saccade directed towards the remembered stimulus location. Eye movements were recorded but not analysed.

The revised Stroop test was performed orally requiring naming of items printed on an A4-size paper. It consists of several subtests; the first one, named congruent test, consists of black words 'grand' and 'petit', organized in four columns on six lines on a white paper. The words were in uppercase or lowercase letters printed, sometimes in bold (see example in Figure 2). The child was asked to read the words as they were written from left to right side from the top to the bottom of the paper, independently to their format (bold, uppercase or lowercase). Then, several incongruent subtests were proposed to the child. For example, the child was invited to read the word 'petit' when the word 'grand' was written or to read the word 'grand' when the word was written in uppercase only or when the word was written in lowercase only. The

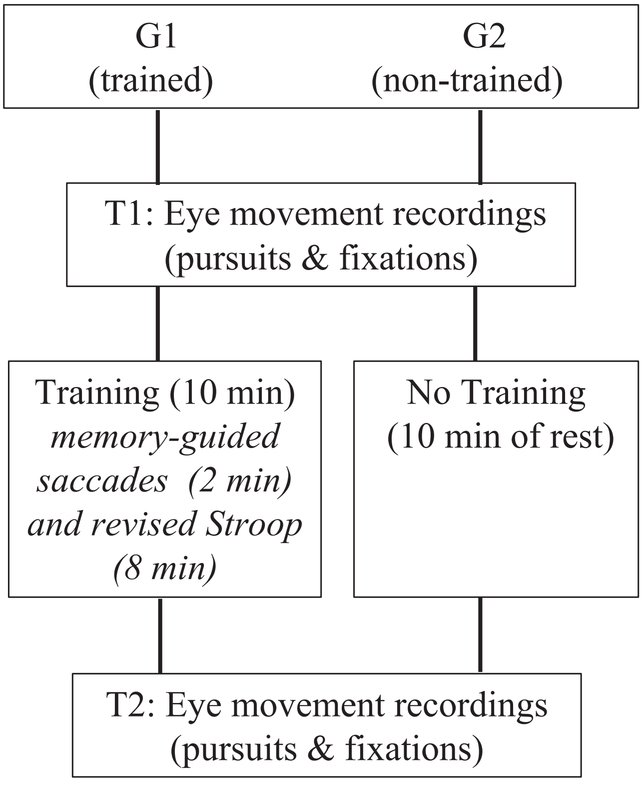


FIGURE 1 Description of trial design.

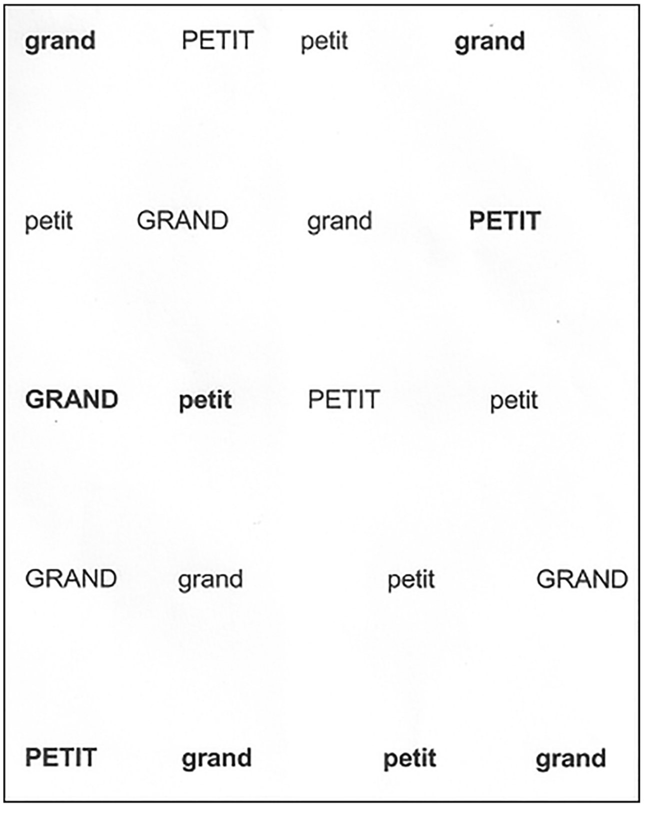


FIGURE 2 Example of the revised Stroop test used for the training.

number of words written on the A4-size paper was then increased following the child's capability.

Firstly, experimenter did some trials with the child in order to be sure that he well understood the test (both congruent and incongruent trials). Then, the training started, lasting for 8 min for the children of G1. After that, another oculomotor recording was performed to estimate the main oculomotor parameters for pursuits and fixation tasks (T2). Children of G2 were not trained, and the second oculomotor measure (T2) was done after a 10-min rest.

2.6 | Data analysis

Calibration factors for each eye were determined by using the eye positions during the calibration procedure (for more details, see Bucci et al., 2012). Eye movement analyses were performed using the MeyeAnalysis software, which automatically determined the onset and the end of each saccade by using a built-in saccade detection algorithm and visually inspected and verified by the investigator. Detection of saccades during pursuit was based on criteria of minimum amplitude (2°) and velocity (30°/s). Catch-up saccades were defined as saccades in the target direction that served to reduce position error and to bring the eye closer to the target. The number of catch-up saccades was counted for each trial. Pursuit gain corresponds to the relationship between the speed of the eye and the speed of the target, and it was obtained by dividing eye velocity by target velocity for each trial. If its value is around 1, it means that the correspondence between the target and the eye is perfect. Scores were then averaged across trials for each test. For both fixation conditions (simple fixation and fixation with distractor), we counted the number of saccades done during the paradigm. All saccades ≥2° were counted given that it is well known that micro-saccades are normally of smaller amplitude (for more details, see Tiadi et al., 2016).

2.7 | Statistical analysis

Oculomotor parameters and the score of the ADOS and ADI-R evaluations were examined in all participants with Pearson correlation coefficients (significant *p*-value below 0.05). ANOVA was run between the two groups (G1 and G2) of children with ASD on oculomotor parameters (gain and number of catch-up saccades during pursuits and number of saccades during fixations) recorded two times (T1 and T2). Post hoc comparisons were made with Bonferroni's method. Significance was considered when the *p*-value was below 0.05. All statistical analyses were processed using JASP software (a free and open-source program for statistical analysis supported by the University of Amsterdam).

3 | RESULTS

In order to explore further the relationship between the clinical characteristic of children with ASD and oculomotor performance, we evaluated the correlation between the scores from the ADOS and ADI-R evaluations and oculomotor performances in pursuits and fixations. We observed a positive correlation only between restricted and repetitive behaviour (RRB) scores of both ADOS and ADI-R and the number of saccades during the fixation task. As shown in Figure 3, both correlations were significant ($R^2 = 0.23$, $p < 0.001$ and $R^2 = 0.08$, $p < 0.04$, respectively for the RRB score of the ADOS and ADI-R).

Figure 4 shows the mean number of catch-up saccades recorded during pursuit eye movements for both groups of children examined (G1 and G2) at T1 and T2.

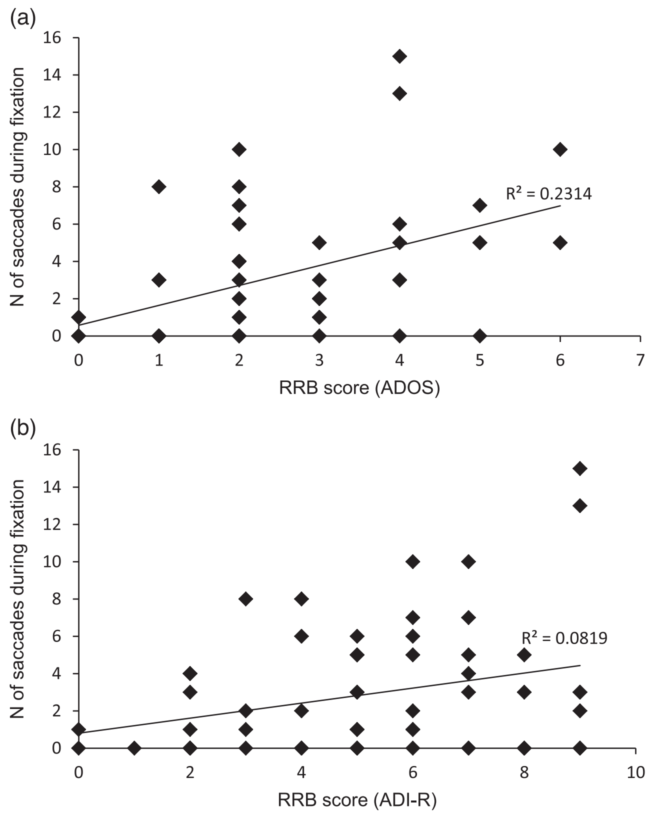


FIGURE 3 Person correlation between the restricted and repetitive behaviour score from the Diagnostic Observation Schedule (ADOS) (a) and the Autism Diagnostic Interview-Revised (ADI-R) (b) and the number of saccades during the fixation task made by all children with autism spectrum disorder (ASD) who participated in the study.

FIGURE 4 Mean and standard deviations of the number of catch-up saccades during pursuit movements for the two groups of children (G1 and G2) at T1 and T2.

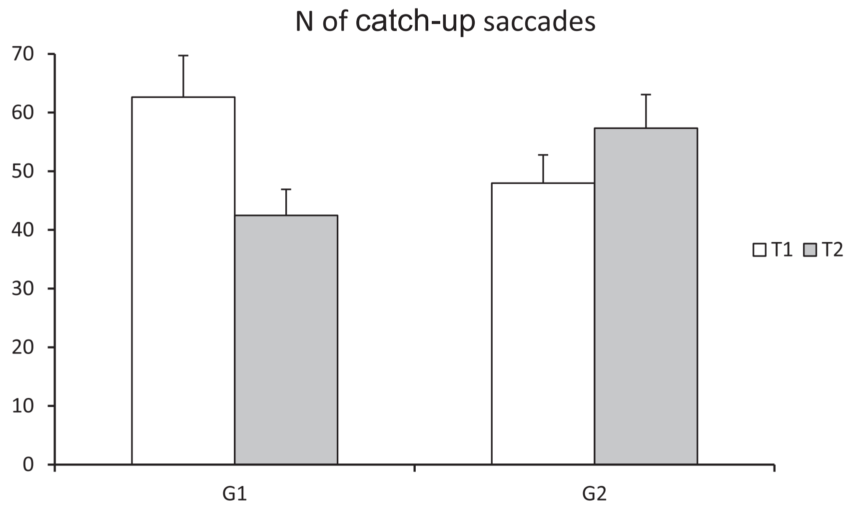
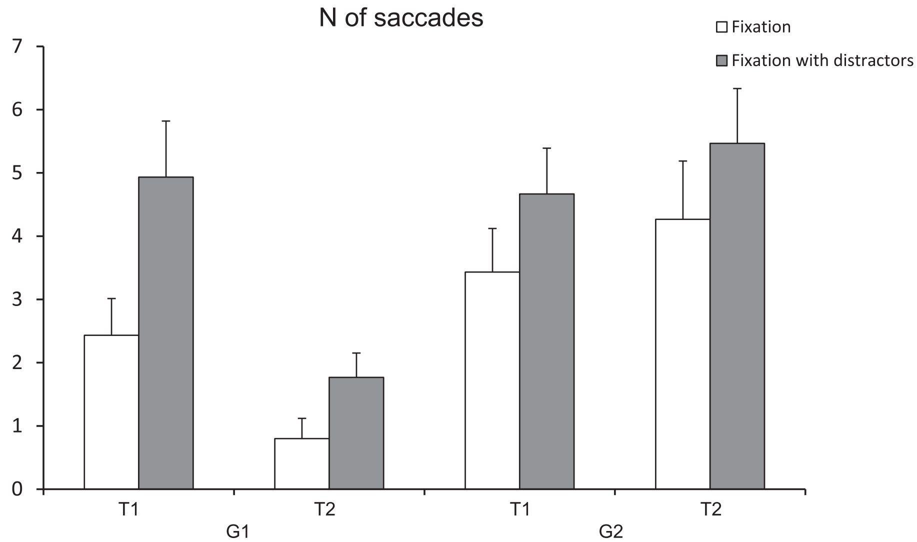


FIGURE 5 Mean and standard deviations of the number of saccades during the fixation task (simple and with distractor) made by the two groups of children (G1 and G2) at T1 and T2.



ANOVA reported a significant interaction $G \times T$ ($F_{[1,56]} = 24.91$, $p < 0.01$, $\eta = 0.06$). Bonferroni post hoc test showed that the number of catch-up saccades decreased significantly ($p < 0.001$) in T2 for the group of children that underwent cognitive training (G1). The gain of pursuits failed to show any significant difference between the two groups of children at T1 (mean 0.89 ± 0.02 and 0.93 ± 0.04 for G1 and G2 respectively) or T2 (mean 0.95 ± 0.03 and 0.91 ± 0.04 for G1 and G2 respectively).

The number of saccades made during fixation task (simple and with distractor) is shown in Figure 5. ANOVA reported a significant interaction $G \times T$ ($F_{[1,56]} = 37.36$, $p < 0.001$, $\eta = 0.03$). Bonferroni post hoc test showed that the number of saccades in T2 for the group of children who underwent cognitive training was significantly lower with respect to the number of saccades observed in T1 respectively in the fixation task ($p < 0.01$) and in the fixation with distractors task ($p < 0.001$). There was also a significant task effect ($F_{[1,56]} = 324.56$, $p < 0.001$, $\eta = 0.03$); indeed, saccades occurred more frequently in the fixation with distractor condition than in the simple fixation task.

4 | DISCUSSION

The first new finding of the present study is that the clinical characteristic of children with ASD, particularly their RRBs measured by ADOS as well as ADI-R evaluations, was positively correlated with the number of saccades during the fixation task. In other words, the more these children have RRB characteristics, the more they show inhibition and attentional deficits. Several studies advanced the hypothesis of a relationship between elevated RRB levels and executive function impairments in children with ASD (Lopez et al., 2005), inhibitory control (Mosconi et al., 2009), cognitive flexibility and working memory (Van Eylen et al., 2015). In other words, the behavioural inflexibility or cognitive deficiencies could be tested by the RRBs as suggested by Mosconi et al. (2009).

A recent review from Tian et al. (2022) described neuroimaging studies showing some abnormalities of the cortico-striatal-thalamo-cortical circuit in relationship with severity of RRBs; consequently, the correlation we observed with poor fixation capabilities could be due to such cortical network that is well known also involved in oculomotor performances (Jarvstad & Gilchrist, 2019). Lidstone et al. (2021) showed aberrant connectivity between the cerebellum and cerebral cortex in 105 children with ASD and found that elevated RRBs were associated with low right posterior cerebellum-left inferior parietal lobule connectivity and high right posterior cerebellar-right connectivity. A recent study of McKinney et al. (2022) reported a relationship between the clinical score of RRB and the white matter volume of the right cerebellar consistent with the well-known role of the cerebellum in the modulation of cognitive and social functions; interestingly, such areas control also eye fixation and pursuit movements (Shemesh & Zee, 2019).

Based on this knowledge, we could advance the hypothesis that oculomotor performances, objectively recorded, together with the classical clinical subjective tests would be used for a better diagnostic of children with neurodevelopmental disorders. In other words, both tools could be used as biomarkers for ASD even if further studies on a larger number of subjects will be necessary. Clinicians could take advance to have different tools available for an easier and better screening of subjects with ASD.

Secondly, the goal of the present study was to evaluate the impact of a short cognitive training rehabilitation on oculomotor performance in children with ASD. After this training type, we reported an improvement in pursuit and fixation capabilities for these children; particularly, children decreased significantly the number of saccades made during both pursuit and fixation tasks.

Our findings are in line with studies cited in Section 1, showing that cognitive training rehabilitation is able to improve inhibitory and attentional functions objectively recorded by a better performance in pursuit and fixation tasks. Indeed, as reported by Kim et al. (2018), cognitive functions involve several domains such as attention, executive function, learning and memory, language, perceptual-motor and social cognition. The present study explored oculomotor functions that are related to some of these capabilities and reported enhancement of some types of eye movements that are related to specific cortical areas. Indeed, it is well known that unwanted saccades in pursuit and fixation tasks could be due to a deficit in prefrontal and fronto-striatal circuits (Leigh & Zee, 2015). In the meta-analysis of Johnson et al. (2016), it has been reported that subjects with ASD showed altered eye movement's behaviour, particularly difficulty in inhibiting saccades during fixations and pursuits, suggesting the presence in subjects with ASD of impairment in the prefrontal cortex and in the anterior cingulate cortex activity. Moreover, Voorhies et al. (2018) in a resting state functional magnetic resonance imaging (MRI) study compared the inhibitory control networks in children with ASD and in typically developing children. These authors found an aberrant functional connectivity between inferior frontal junction and key regions supportive of inhibitory control, like middle frontal gyrus, superior parietal lobule and caudate in children with ASD, supporting the hypothesis of a delayed maturation inhibitory control networks in these kinds of patients.

In line with all these findings, we could suggest that cognitive training rehabilitation, albeit brief, could modify brain structures leading to a better inhibitory control and attentional engagement in children with ASD.

5 | CONCLUSION

The present study is the first one to test the benefit of a short cognitive training rehabilitation on oculomotor performances in children with ASD. Children with ASD are in fact able to improve their oculomotor performances after a short cognitive training rehabilitation. However neuroimaging studies are necessary to explore deeply the relationship between oculomotor performances, executive functions, autism and brain network. Moreover in order to state our conclusions, it is necessary to carry out longitudinal studies with the aim of observing whether these improvements are maintained over time. Finally, the presence of a positive correlation between RRBs and the number of saccades during the fixation task suggested the interest in combining clinical assessment and eye movement's studies in order to improve the diagnostic and the eventual re-education of children with neurodevelopmental disorders.

AUTHOR CONTRIBUTIONS

Conceptualization: Simona Caldani and Maria Pia Bucci. Selection of patients: Elise Humeau and Richard Delorme. Measures and data analysis: Simona Caldani and Maria Pia Bucci. Writing original draft: Simona Caldani, Maria Pia Bucci and Richard Delorme. Review and editing: Elise Humeau.

ACKNOWLEDGEMENTS

The authors thank the children who participated in the study. The authors also thank the practitioners from the

Child and Adolescent Psychiatry Department (Robert Debré Hospital).

CONFLICT OF INTEREST STATEMENT

The authors have no financial relationships relevant to this article to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

This work shows that eye movement's recording is an objective and simple tool to understand cortical network dysfunctions in children with ASD, in particular attention and inhibition capabilities. This study for the first time reported also a correlation between eye movement's performance and clinical symptoms such as the restricted and repetitive behaviour (RRB) score measured by ADOS as well as ADI-R evaluations pointing out the interest in combining eye movement's tests and clinical assessment for a better diagnostic and evaluation of children with ASD. In the present study, we reported also that a short cognitive re-education is able to improve inhibition and attentional capabilities in these types of children. This kind of re-education could be used by clinicians and therapeutics for children with ASD.

ORCID

Maria Pia Bucci https://orcid.org/0000-0001-6673-2026

REFERENCES

American Psychiatric Association APA. (2013). *Diagnostic and statistical manual of mental disorders* (DSM 5th ed.). https://doi.org/10.1176/appi.books.9780890425596

Bremer, E., Graham, J. D., Heisz, J. J., & Cairney, J. (2020). Effect of acute exercise on prefrontal oxygenation and inhibitory control among male children with autism spectrum disorder: An exploratory study. *Frontiers in Behavioral Neuroscience*, *14*, 84. https://doi.org/10.3389/fnbeh.2020.00084

Bucci, M. P., Nassibi, N., Gerard, C.-L., Bui-Quoc, E., & Seassau, M. (2012). Immaturity of binocular saccade coordination in dyslexic children: Evidence from a reading and visual search study. *PlosOne*, *7*(3), e33458. https://doi.org/10.1371/journal.pone.0033458

Budde, H., Voelcker-Rehage, C., Pietrabyk-Kendziorra, S., Ribeiro, P., & Tidow, G. (2008). Acute coordinative exercise improves attentional performance in adolescents. *Neuroscience Letters*, *441*, 219–223. https://doi.org/10.1016/j.neulet.2008.06.024

Caldani, S., Humeau, E., Delorme, R., & Bucci, M. P. (2022). Memory guided saccades in children with autism spectrum disorder. *Applied Neuropsychology: Child*, *1-6*, 131–136. https://doi.org/10.1080/21622965.2022.2042300

Caldani, S., Razuk, M., Septier, M., Barela, J. A., Delorme, R., Acquaviva, E., & Bucci, M. P. (2019). The effect of dual task on attentional performance in children with ADHD. *Frontiers in Integrative Neuroscience*, *12*, 67. https://doi.org/10.3389/fnint.2018.00067

Chukoskie, L., Westerfield, M., & Townsend, J. (2018). A novel approach to training attention and gaze in ASD: A feasibility and efficacy pilot study. *Developmental Neurobiology*, *78*(5), 546–554. https://doi.org/10.1002/dneu.22563

Dandil, Y., Smith, K., Kinnaird, E., Toloza, C., & Tchanturia, K. (2020). Cognitive remediation interventions in autism spectrum condition: A systematic review. *Frontiers in Psychiatry*, *11*, 722. https://doi.org/10.3389/fpsyt.2020.00722

Eack, S. M., Hogarty, S. S., Greenwald, D. P., Litschge, M. Y., Porton, S. A., Mazefsky, C. A., & Minshew, N. J. (2018). Cognitive enhancement therapy for adult autism spectrum disorder: Results of an 18-month randomized clinical trial. *Autism Research*, *11*(3), 519–530. https://doi.org/10.1002/aur.1913

Fiefer, S. G., & Rattan, G. (2007). Executive functioning skills in male students with social emotional disorders. *International Journal of Neuroscience*, *117*(11), 1565–1577. https://doi.org/10.1080/00207450701239350

Fiske, A., & Holmboe, K. (2019). Neural substrates of early executive function development. *Developmental Review*, *52*, 42–62. https://doi.org/10.1016/j.dr.2019.100866

Geurts, H. M., van den Bergh, S. F., & Ruzzano, L. (2014). Prepotent response inhibition and interference control in autism spectrum disorders: Two meta-analyses. *Autism Research*, *7*(4), 407–420. https://doi.org/10.1002/aur.1369

Ha, S., Sohn, I. J., Kim, N., Sim, H. J., & Cheon, K. A. (2015). Characteristics of brains in autism spectrum disorder: Structure, function and connectivity across the lifespan. *Exp Neurobiol*, *24*(4), 273–284. https://doi.org/10.5607/en.2015.24.4.273

Hajri, M., Abbes, Z., Yahia, H. B., Jelili, S., Halayem, S., Mrabet, A., & Bouden, A. (2022). Cognitive deficits in children with autism spectrum disorders: Toward an integrative approach combining social and non-social cognition. *Frontiers in Psychiatry*, *13*, 917121. https://doi.org/10.3389/fpsyt.2022.917121

Izawa, Y., & Suzuki, H. (2014). Activity of fixation neurons in the monkey frontal eye field during smooth pursuit eye movements. *Journal of Neurophysiology*, *112*(2), 249–262. https://doi.org/10.1152/jn.00816.2013

Jarvstad, A., & Gilchrist, I. D. (2019). Cognitive control of saccadic selection and inhibition from within the core cortical saccadic network. *The Journal of Neuroscience*, *39*(13), 2497–2508. https://doi.org/10.1523/JNEUROSCI.1419-18.2018

Johnson, B. P., Lum, J. A., Rinehart, N. J., & Fielding, J. (2016). Ocular motor disturbances in autism spectrum disorders: Systematic review and comprehensive meta-analysis. *Neuroscience and Biobehavioral Reviews*, *69*, 260–279. https://doi.org/10.1016/j.neubiorev.2016.08.007

Kenworthy, L., Anthony, L. G., Naiman, D. Q., Cannon, L., Wills, M. C., Luong-Tran, C., Werner, M. A., Alexander, K. C., Strang, J., Bal, E., Sokoloff, J. L., & Wallace, G. L. (2014). Randomized controlled effectiveness trial of executive function intervention for children on the autism spectrum. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *55*(4), 374–383. https://doi.org/10.1111/jcpp.12161

Kim, E. J., Bahk, Y. C., Oh, H., Lee, W. H., Lee, J. S., & Choi, K. H. (2018). Current status of cognitive remediation for psychiatric disorders: A review. *Frontiers in Psychiatry*, *9*, 461. https://doi.org/10.3389/fpsyt.2018.00461

Leigh, R. J., & Zee, D. S. (2015). *The neurology of eye movements* (5ème ed.). Oxford University Press. https://doi.org/10.1093/med/9780199969289.001.0001

Lidstone, D. E., Rochowiak, R., Mostofsky, S. H., & Nebel, M. B. (2021). A data driven approach reveals that anomalous motor system connectivity is associated with the severity of core autism symptoms. *Autism Research*, *2021*, 2476. https://doi.org/10.1002/aur.2476

Lions, C., Bui-Quoc, E., Wiener-Vacher, S., Seassau, M., & Bucci, M. P. (2013). Smooth pursuit eye movements in children with strabismus and in children with vergence deficits. *PLoS ONE*, *8*, e83972. https://doi.org/10.1371/journal.pone.0083972

Lopez, B. R., Lincoln, A. J., Ozonoff, S., & Lai, Z. (2005). Examining the relationship between executive functions and restricted, repetitive symptoms of autistic disorder. *Journal of Autism and Developmental Disorders*, *35*, 445–460. https://doi.org/10.1007/s10803-005-5035-x

McKinney, W. S., Kelly, S. E., Unruh, K. E., Shafer, R. L., Sweeney, J. A., Styner, M., & Mosconi, M. W. (2022). Cerebellar volumes and sensorimotor behavior in autism spectrum disorder. *Frontiers in Integrative Neuroscience*, *16*, 821109. https://doi.org/10.3389/fnint.2022.821109

Miranda, A., Berenguer, C., Roselló, B., Baixauli, I., & Colomer, C. (2017). Social cognition in children with high-functioning autism spectrum disorder and attention-deficit/hyperactivity disorder associations with executive functions. *Frontiers in Psychology*, *8*, 1035. https://doi.org/10.3389/fpsyg.2017.01035

Morgan, L., Hooker, J. L., Sparapani, N., Reinhardt, V. P., Schatschneider, C., & Wetherby, A. M. (2018). Cluster randomized trial of the classroom SCERTS intervention for elementary students with autism spectrum disorder. *Journal of Consulting and Clinical Psychology*, *86*(7), 631–644. https://doi.org/10.1037/ccp0000314

Mosconi, M. W., Kay, M., D'Cruz, A. M., Seidenfeld, A., Guter, S., Stanford, L. D., & Sweeney, J. A. (2009). Impaired inhibitory control is associated with higher-order repetitive behaviors in autism spectrum disorders. *Psychological Medicine*, *39*, 1559–1566. https://doi.org/10.1017/S0033291708004984

Ozonoff, S., Pennington, B. F., & Rogers, S. J. (1991). Executive function deficits in high functioning autistic individuals: Relationship to theory of mind. *Journal of Child Psychology and Psychiatry*, *32*, 1081–1105. https://doi.org/10.1111/j.1469-7610.1991.tb00351.x

Pastor-Cerezuela, G., Fernández-Andrés, M. I., Sanz-Cervera, P., & Marín-Suelves, D. (2020). The impact of sensory processing on executive and cognitive functions in children with autism spectrum disorder in the school context. *Research in Developmental Disabilities*, *96*, 103540. https://doi.org/10.1016/j.ridd.2019.103540

Pereira, A. M., Campos, B. M., Coan, A. C., Pegoraro, L. F., de Rezende, T. J. R., Obeso, I., Dalgalarrondo, P., da Costa, J. C., Dreher, J. C., & Cendes, F. (2018). Differences in cortical structure and functional MRI connectivity in high functioning autism. *Frontiers in Neurology*, *9*, 539. https://doi.org/10.3389/fneur.2018.00539

Rommelse, N. N., Van der Stigchel, S., & Sergeant, J. A. (2008). A review on eye movement studies in childhood and adolescent psychiatry. *Brain and Cognition*, *268*(3), 391–414. https://doi.org/10.1016/j.bandc.2008.08.025

Schmidt, M., Benzing, V., & Kamer, M. (2016). Classroom-based physical activity breaks and children's attention: Cognitive engagement works. *Frontiers in Psychology*, *7*, 1474. https://doi.org/10.3389/fpsyg.2016.01474

Schmitt, L. M., White, S. P., Cook, E. H., Sweeney, J. A., & Mosconi, M. W. (2018). Cognitive mechanisms of inhibitory control deficits in autism spectrum disorder. *Journal of Child Psychology and Psychiatry*, *59*(5), 586–595. https://doi.org/10.1111/jcpp.12837

Shemesh, A. A., & Zee, D. S. (2019). Eye movement disorders and the cerebellum. *Journal of Clinical Neurophysiology*, *36*(6), 405–414. https://doi.org/10.1097/WNP.0000000000000579

Takarae, Y., Minshew, N. J., Luna, B., Krisky, C. M., & Sweeney, J. A. (2004). Pursuit eye movement deficits in autism. *Brain*, *127*(pt 12), 2584–2594. https://doi.org/10.1093/brain/awh307

Takarae, Y., Minshew, N. J., Luna, B., & Sweeney, J. A. (2007). Atypical involvement of frontostriatal systems during sensorimotor control in autism. *Psychiatry Research: Neuroimaging*, *156*, 117–127.

Tiadi, A., Gérard, C. L., Peyre, H., Bui-Quoc, E., & Bucci, M. P. (2016). Immaturity of visual fixations in dyslexic children. *Frontiers in Human Neuroscience*, *10*, 58. https://doi.org/10.3389/fnhum.2016.00058

Tian, J., Gao, X., & Yang, L. (2022). Repetitive restricted behaviors in autism spectrum disorder: From mechanism to development of therapeutics. *Frontiers in Neuroscience*, *16*, 780407. https://doi.org/10.3389/fnins.2022.780407

Tiego, J., Testa, R., Bellgrove, M. A., Pantelis, C., & Whittle, S. (2018). A hierarchical model of inhibitory control. *Frontiers in Psychology*, *9*, 1339. https://doi.org/10.3389/fpsyg.2018.01339

Van den Bergh, S. F., Scheeren, A. M., Begeer, S., Koot, H. M., & Geurts, H. M. (2014). Age related differences of executive functioning problems in everyday life of children and adolescents in the autism spectrum. *Journal of Autism and Developmental Disorders*, *44*(8), 1959–1971. https://doi.org/10.1007/s10803-014-2071-4

Van Eylen, L., Boets, B., Steyaert, J., Wagemans, J., & Noens, I. (2015). Executive functioning in autism spectrum disorders: Influence of task and sample characteristics and relation to symptom severity. *European Child & Adolescent Psychiatry*, *24*, 1399–1417. https://doi.org/10.1007/s00787-015-0689-1

Vogan, V. M., Leung, R. C., Safar, K., Martinussen, R., Smith, M. L., & Taylor, M. J. (2018). Longitudinal examination of everyday executive functioning in children with ASD: Relations with social, emotional, and behavioral functioning over time. *Frontiers in Psychology*, *9*, 1774. https://doi.org/10.3389/fpsyg.2018.01774

Voorhies, W., Dajani, D. R., Vij, S. G., Shankar, S., Turan, T. O., & Uddin, L. Q. (2018). Aberrant functional connectivity of inhibitory control networks in children with autism spectrum disorder. *Autism Research*, *11*(11), 1468–1478. https://doi.org/10.1002/aur.2014

How to cite this article: Caldani, S., Humeau, E., Delorme, R., & Bucci, M. P. (2023). Inhibition functions can be improved in children with autism spectrum disorders: An eye-tracking study. *International Journal of Developmental Neuroscience*, 1–11. https://doi.org/10.1002/jdn.10276