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Does differential visual exploration contribute to visual memory impairments in 22q11.2 microdeletion syndrome?

M. Bostelmann,[1,2] B. Glaser,[1] A. Zaharia,[1,3] S. Eliez[1,4] & M. Schneider[1,5]

1 *Department of Psychiatry, Office Médico-Pédagogique, Research Unit, University of Geneva School of Medicine, Geneva, Switzerland*
2 *Laboratory of Brain and Cognitive Development, Institute of Psychology, University of Lausanne, Lausanne, Switzerland*
3 *Swiss Center for Affective Sciences, University of Geneva, Geneva, Switzerland*
4 *Department of Genetic Medicine and Development, University of Geneva School of Medicine, Geneva, Switzerland*
5 *Center for Contextual Psychiatry, Department of Neuroscience, KU Leuven, Leuven, Belgium*

Abstract

Background Chromosome 22q11.2 microdeletion syndrome (22q11.2DS) is a genetic syndrome characterised by a unique cognitive profile. Individuals with the syndrome present several non-verbal deficits, including visual memory impairments and atypical exploration of visual information. In this study, we seek to understand how visual attention may contribute to memory difficulties in 22q11.2DS by tracking eye movements during the encoding phase of a visual short-term memory task.

Method Eye movements were recorded during a computerised version of the multiple-choice Benton Visual Retention Test, which consisted of exploring and then recognising complex visual stimuli. Seventy-four participants affected by 22q11.2DS were compared with 70 typically developing participants.

Results Participants with 22q11.2DS performed less well than healthy controls on the task and spent more time and fixations on the principal (larger central) figures and less time and fixations on the smaller peripheral figures within the stimuli.

Conclusions This study is the first to investigate visual attention in 22q11.2DS during a memory task. The results delineate impaired processes during encoding that affect visual memory performance. The findings may be especially useful for informing interventions intended to boost visual learning in patients with 22q11.2DS.

Keywords 22q11.2 microdeletion syndrome, encoding, eye movements, visual attention, visual short-term memory

Introduction

Chromosome 22q11.2 deletion syndrome (22q11.2DS), also known as DiGeorge syndrome, is a neurodevelopmental disorder resulting from a hemizygotic interstitial deletion on the q11 band of chromosome 22. The prevalence of the syndrome falls between 1 in 2000–4000 live births (Oskarsdottir *et al.* 2004; Shprintzen 2008). Individuals often present physical abnormalities, such as velopharyngeal, facial dysmorphology and cardiac problems, although the phenotype of the deletion is highly variable (Shprintzen 2008). While persons with 22q11.2DS show intellectual functioning in the

Correspondence: Ms. Mathilde Bostelmann Department of Psychiatry, Office Médico-Pédagogique, Research Unit, University of Geneva School of Medicine, Geneva, Switzerland (e-mail: mathilde.bostelmann@unil.ch).

borderline range (Antshel *et al.* 2008), a specific profile of cognitive impairments associated with the syndrome has been delineated over the last two decades. Neuropsychological studies of 22q11.2DS have reported several learning difficulties within the non-verbal domain, including visuo-perceptual, visual discrimination and emotion recognition impairments (Swillen *et al.* 1999; Henry *et al.* 2002; Campbell *et al.* 2011).

The learning and subsequent retention of visual information during a short delay (i.e. visual short-term memory) is thought to be especially impaired in 22q11.2DS. Patients with 22q11.2DS have difficulties memorising faces, shapes, spatial localisations or geometric designs (Campbell *et al.* 2010; Vicari *et al.* 2012; Gur *et al.* 2014; Bearden *et al.* 2001; Goldenberg *et al.* 2012). However, the aetiology underlying these memory impairments in 22q11.2DS remains unknown. Indeed, standardised tests used in previous studies estimate mnemonic ability but cannot identify the core processes that are impaired (Fletcher *et al.* 1998; Fletcher *et al.* 1998).

Eye movements appear to be especially critical to the encoding of visuospatial information (Pazzaglia *et al.* 2014; Brockmole & Irwin 2005; Pearson & Sahraie 2003). We do not scan visual stimuli randomly; rather, we fixate on specific areas of our visual field and move between these areas to process information (Yang *et al.* 2002; Holmqvist *et al.* 2011; Bojko 2013). In 22q11.2DS, several studies have demonstrated that individuals with 22q11.2DS have atypical visual exploration. Glaser *et al.* (2010) and Campbell *et al.* (2010) showed that affected participants spent less time on the eyes and more time on the mouth compared with healthy subjects during a face discrimination and an emotion recognition task, respectively. Additionally, McCabe *et al.* (2011) showed that patients with 22q11.2DS demonstrated impoverished visual exploration and exhibited fewer fixations on complex visual stimuli (cities and rural scenes depicting different weather conditions) compared with a control group. Fixation patterns are important because they reflect the gathering of visual information into an encoded representation (Tatler *et al.* 2005; Hollingworth & Henderson 2002; Gershberg & Shimamura 1995). The effects of visual exploration on the encoding of visual information have never been studied in 22q11.2DS, but individuals' lower scores on memory tasks may be due to differential visual exploration.

Eye movements also reflect the allocation of attention and serve as a good indicator of focal points (Henderson & Ferreira 2004). Posner and Petersen (1990) first described three subsystems of attention: the *alerting* system maintains optimal vigilance and performance during a task; the *orienting* system refers to the capacity to focus on a particular location in the visual field; and the *executive* component works to inhibit competing inputs. In the context of 22q11.2DS, several studies have shown that visuospatial attention is impaired due to deficits in the executive component, and specifically due to troubles with inhibition (Bish *et al.* 2005, Sobin *et al.* 2004; Simon *et al.* 2005; Simon *et al.* 2005). Given the impact of inhibition on visuospatial attention in general, a lack of inhibition during visual exploration may well impact memory performance in the syndrome. Specifically, increased exploration of certain elements, due to difficulty disengaging attention, could limit the exploration and eventual encoding of other visual elements. The Benton Visual Retention Test (BVRT) (Sivan 1992) is well suited for testing this hypothesis because it requires exploration and recognition of complex geometrical figures, including principal and peripheral elements. Moreover, because a large sample of patients with 22q11.2DS was shown to be impaired on the BVRT stimuli (Bostelmann *et al.* 2016), recording and analysing eye movements during encoding could help to explain poor performance on the BVRT and general problems with visual short-term memory in the syndrome.

In the present study, we investigated visual exploration during the encoding phase of the multiple-choice form of the computerised BVRT (C-BVRT) in a large group of participants with 22q11.2DS and healthy controls. Based on previous studies demonstrating differential patterns of visual exploration in 22q11.2DS compared with typical development (McCabe *et al.* 2011; Campbell *et al.* 2010; Glaser *et al.* 2010), we hypothesised that participants with 22q11.2DS would show atypical exploration during the BVRT. Specifically, compared with control individuals, we expected that 22q11.2DS would have difficulties disengaging their attention from the different parts of the stimuli. We expect a greater number of fixations and more time spent on

the principal elements of the stimuli neglecting the principal parts. However, because no other study has reported eye tracking results from a memory/encoding task, it is also possible that the participants with 22qq1.2DS fixate and spend more time on the peripheral elements neglecting the principal parts of the stimuli. We also postulated that this pattern of exploration would be linked to memory performance. Finally, given the processes underlying visual attention (Petersen & Posner 2012) and impaired inhibition, or disengagement, in individuals with 22q11.2DS, we explored whether either processing speed (as a vigilance indicator) or inhibition may be related to visual exploration in patients with the syndrome.

Method

Participants

A total of 74 participants with 22q11.2DS (39 females, 35 males) with a mean age of 14.6 years (SD = 5.1) were included in the study. The presence of the 22q11.2 microdeletion was confirmed using quantitative fluorescent polymerase chain reaction. At time of testing, 12 (16.2%) participants were taking methylphenidate, five (6.8%) were taking antipsychotics, three (3.6%) were taking antidepressants and one (1.4%) was on antiepileptic medication. Seven (9.5%) individuals had a psychotic disorder, 21 (28.4%) had simple phobia, 19 (26.7%) had attention-deficit/hyperactivity disorder (ADHD), eight (10.8%) had generalised anxiety disorder and two (2.7%) had a major depressive disorder. The control group (TD) consisted of 70 healthy individuals (40 females, 30 males) with a mean age of 15.3 years (SD = 4.5). Half of the TD participants were siblings of participants with 22q11.2DS, and the other half were community controls (50%). Before being included, TD participants were screened to rule out past or present neurological or psychiatric disorders. The TD and 22q11.2DS groups did not differ on age ($t(142) = 0.85$, $P > 0.05$) or gender distribution ($x^2_{(1)} = 0.29$, $P > 0.05$). Participants with 22q11.2DS and TD were recruited by advertising at patient association meetings and in newsletters, as well as through word of mouth. Written informed consent was obtained from both participants and their parents under protocols approved by the Institutional Review Board of the University of Geneva.

Materials

The computerised multiple-choice form of the Benton Visual Retention Test

For eye-tracking exploration, we created a computerised version of the original multiple-choice form of the BVRT. The BVRT by Sivan (1992) is well-suited for populations with intellectual disability or ADHD, such as 22q11.2DS (Snow 1998; Rowley & Baer 1961), given its short duration (less than 5 min). Before beginning the task, participants were told to pay attention and remember each design. Then, each BVRT stimulus was shown for a period of 10 s (encoding phase) followed by a multiple-choice picture composed of four different versions of the stimulus. Participants were asked to choose the one that was previously shown (Fig. 1 choice B). Sivan (1992) described the stimuli of the BVRT as being composed of different parts. Accordingly, designs 3 to 10 are composed of two main geometrical forms (i.e. principal figures) and one smaller peripheral geometrical form positioned near the principal figures (i.e. peripheral figures). Designs 1 and 2 were excluded from the statistical analyses using eye-tracking variables because they contain only one principal figure. To calculate memory performance, a total memory score was computed for each participant (number of correct answers, maximum = 10).

Unlike the paper and pencil task, the multiple choice BVRT was not originally designed with qualitative analysis of errors (Sivan 1992). However, categorising errors can offer important, qualitative insight into the trickiest parts of the stimuli for individuals with 22q11.2DS to encode. For this reason, we distinguished errors involving a principal figure (called *principal errors*) (i.e. Fig. 1 choice A) from errors involving a peripheral figure (called *peripheral errors*) (i.e. Fig. 1 choice C). When it was not possible to determine the type of error committed by a participant, we categorised it as an *unknown error* (i.e. Fig. 1 choice D). For all participants, the C-BVRT was administrated approximately 24 h after the paper and pencil administration of the BVRT, which was described at length in a previous study (Bostelmann *et al.* 2016).

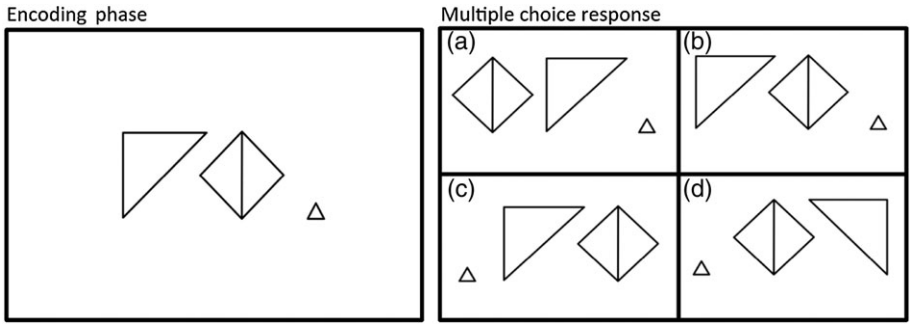

Figure 1 Example of encoding and multiple-choice stimuli from the computerised Benton Visual Retention Test.

The C-BVRT was displayed on a Tobii 1750 eye tracker with a 17-inch display (www.tobii.com) using Clearview 2.7.1 software. Maximum resolution for the screen was 1280 × 1024 pixels, and the sample rate was 60 Hz. The Tobii system accounted for head movements up to 60 cm away from the device. Therefore, participants were positioned at a distance of less than 60 ± 10 cm from the screen. A 5-points calibration procedure was performed before initialising the C-BVRT to ensure that participants' movements were recordable at all distinct points on the screen for both eyes. Per Tobii system and in accordance with previous studies, fixations were defined by a gaze durations of at least 100 ms within a circle measuring 30 pixels in diameter (Glaser *et al.* 2010; Franchini *et al.* 2016). The stimuli were divided into three regions of interest (ROIs): ROI total, ROI principal figures and ROI peripheral figures (Fig. 2) to categorise eye movements during the encoding phase. Using data from the encoding phase only, three variables were calculated for each ROI of designs 3 to 10: *number of fixations*, *total time spent* and *average fixation duration*. A ratio was then computed by dividing the number of fixations on the peripheral figures by the number of fixations on the principal figures (*number of fixations ratio*). Similar ratios were calculated for total time spent (*total time spent ratio*) and average fixation duration (*average duration fixation ratio*). Smaller ratios indicate less time/fixations on peripheral figures compared with principal figures.

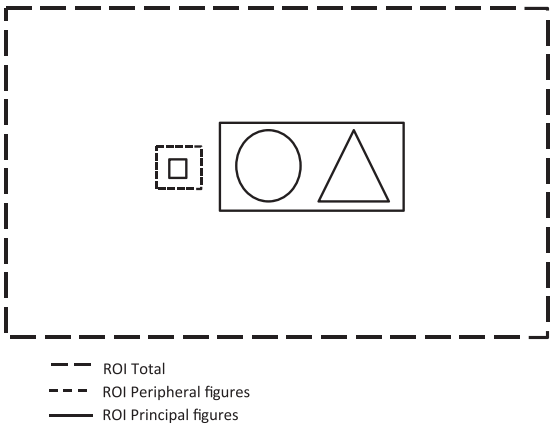

Figure 2 Regions of interest (ROIs).

Assessment of general intellectual functioning and reasoning abilities

The Wechsler Intelligence Scale for Children, Third Edition (Wechsler 1991), was used to assess participants younger than 17 years old and the Wechsler Adult Intelligence Scale-III (Wechsler 1997) was administered to adult participants. Both batteries generate a verbal intellectual quotient (VIQ) and a non-verbal or performance intellectual quotient (PIQ). In this study, we also used Processing Speed Index (PSI) to evaluate participants' ability to process visual information successfully and rapidly.

Inhibition

The Conner's Continuous Performance Test (CPT) (Conners & Staff 2000) was used as a measure of inhibition. In this computerised task, participants were told to press a button each time they saw a letter on the screen. When they saw an 'X', they needed to inhibit their response by not pressing the button. Three variables are generally considered as reliable indicators of inhibition: the number of commission errors (i.e. an erroneous response to a non-target or

pressing for a letter that was not an 'X'), the number of perseverations (a response occurring less than 100 ms after a stimulus, pressing more than 100 ms after the appearance of an 'X') and the hit reaction time (mean response time in milliseconds for correct responses). Standardised T scores were used in this study. Data for the CPT were not available for two participants with 22q11.2DS.

Data analysis

Data for each participant were first inspected, and values three standard deviations below the means were excluded from the study. As a result, participants with extreme results on both memory and eye tracking variables (average duration, total time spent and number of fixations on the ROI's) were excluded from the data. During the encoding phase of the stimuli, individuals with 22q11.2DS spend less time on the computer screen compared with the TD group (M_{TD} = 38.35 s, $M_{22q11.2DS}$ = 35.38 s, $t(142) = 2.77$, $P = 0.006$, $\eta^2 = 0.05$). The following are two possible explanations for this difference: First, the quality of the recording may have been compromised by excess movement by the participants, especially in the 22q11.2DS group given the high prevalence of ADHD (Schneider *et al.* 2014, Antshel *et al.* 2006). Second, many individuals with 22q11.2DS wear glasses, which can impact data recording. Given this difference in on-screen time, we used percentages in our analyses that were calculated by dividing the number of fixations in each ROI by the total number of fixations on the screen multiplied by 100. We also calculated the percentage of total time spent on each ROI by dividing the time spend on each ROI by the total time spent on the screen multiplied by 100.

Independent *t*-tests were used to run between-group comparisons for the number of fixations ratio. Non-parametric Mann–Whitney *U*-tests were used for between-group comparisons for the average fixation duration and total time spent ratios because they violated normality assumptions. Group comparisons on memory and inhibition were also conducted with Mann–Whitney *U*-tests and IQ scores via *t*-tests. Group differences in the number of errors on the C-BVRT were tested using Tobit regressions and chi-squared tests because the distributions were highly skewed (for both the TD and 22q11.2DS groups). Finally, to investigate whether visual exploration may be linked to the cognitive variables per our hypothesis, we used Spearman correlations to test whether the three visual exploration ratios were related to memory performance or other cognitive measures (inhibition and speed of processing). Benjamini–Hochberg corrections for multiple comparisons were applied to all results (Thissen *et al.* 2002).

Results

Visual exploration on the principal and peripheral figures regions of interest

Between-group comparisons of the calculated ratios (fixations on the peripheral figures divided by fixations on the principal figures) revealed that individuals with 22q11.2DS had smaller ratios for number of fixations ($t(142) = 5.81$, $P < 0.001$, $\eta^2 = 0.19$), time spent ($Mdn_{TD} = 0.26$, $Mdn_{22q11.2DS} = 0.13$, $U = 1260.00$, $z = -5.32$, $P < 0.001$, $r = -0.44$) and average fixation duration ($Mdn_{TD} = 1.08$, $Mdn_{22q11.2DS} = 0.93$, $U = 1961.00$, $z = -2.51$, $P = 0.01$, $r = -0.21$) compared with TD (Table 1). These results indicate that individuals with 22q11.2DS focused more attention on the principal figures compared with the TD group.

Memory performance and types of errors

The 22q11.2DS group had lower total C-BVRT scores than TD participants ($Mdn_{TD} = 9.0$, $Mdn_{22q11.2DS} = 8.0$, $U = 1079.0$, $z = -6.21$, $P < 0.001$, $r = -0.51$) (Table 2). Tobit regressions revealed a significant effect of diagnosis on the number of principal and peripheral errors (Table 3), indicating that the 22q11.2DS group made more peripheral and more principal errors compared with TD. Figure 3 shows the proportion of individuals with at least one principal error or one peripheral error. All participants made a maximum of two principal errors and two peripheral errors. The proportion of individuals who made principal versus peripheral errors was identical between groups ($x^2_{(1)} = 0.60$, $P > 0.05$).

Associations between visual exploration, memory and inhibition measures

In the 22q11.2DS group, correlation analyses showed that the average fixation duration ratio was related

Table 1 Eye-tracking ratios for the 22q11.2DS and TD groups

	TD (*N* = 70)		22q11.2DS (*N* = 74)			
	Mean	SD	Mean	SD	Statistical difference	Effect size
Ratios						
Ratio: number of fixations	0.24	0.10	0.15	0.08	$P < 0.001$	$\eta^2 = 0.19$
Ratio: total time spent	0.26	0.13	0.15	0.09	$P < 0.001$	$r = -0.44$
Ratio: average fixation duration	1.09	0.25	1.01	0.45	$P = 0.012$	$r = -0.21$

Effect size for the non-parametric statistical tests (*r*) was calculated according to Rosenthal's equation (Rosenthal 1991).

Table 2 Mean (SD) for the cognitive measures

	TD (*N* = 70)	22q11.2DS (*N* = 74)	Statistical difference	Effect size
General intellectual functioning	Mean (SD)	Mean (SD)		
FSIQ	111.04 (13.87)	70.13 (10.85)	$P < 0.001$	$\eta^2 = 0.73$
VIQ	110.62 (13.69)	76.63 (13.59)	$P < 0.001$	$\eta^2 = 0.61$
PIQ	108.58 (13.86)	69.14 (10.90)	$P < 0.001$	$\eta^2 = 0.72$
Speed information processing (PSI)	108.58 (13.30)	79.36 (16.54)	$P < 0.001$	$\eta^2 = 0.49$
Memory C-BVRT total score	9.1 (1)	7.5 (1.7)	$P < 0.001$	$r = -0.51$
Inhibition *t*-scores	TD (*N* = 70)	22q11.2DS (*N* = 72)		
	Mean (SD)	Mean (SD)		
Number of commission errors	50.11 (11.89)	53.65 (11.37)	NS	
Number of perseverations	49.32 (8.33)	56.46 (21.58)	NS	
Hit reaction time (ms)	42.99 (9.71)	46.25 (11.04)	NS	

Effects size for the non-parametric statistical tests (*r*) was based on Rosental's equation (Rosenthal 1991). FSIQ, full-scale intellectual quotient; PIQ, performance intellectual quotient; PSI, Processing Speed Index; VIQ, verbal intellectual quotient.

Table 3 Results from the Tobit regressions with diagnosis (22q11.2DS and TD individuals) as the independent variable and number of errors as the dependent variable (either principal or peripheral errors)

	Coefficient	95% confidence interval	*t*-statistic	Significance
Regression 1: number of principal errors	b = 0.9	0.11–1.69	2.26	0.03
Regression 2: number of peripheral errors	b = 1.07	0.50–1.64	0.29	<0.001

to the total memory score from the C-BVRT ($r = 0.30$, $P = 0.009$). Significant correlations were not observed between memory performance and the number of fixations ratio ($r = 0.32$, $P > 0.05$) or between memory performance and the total time spent ratio ($r = 0.11$, $P > 0.05$). We did not detect a correlation between inhibition measures (number of commission errors, number of perseverations and hit reaction times from the CPT) and any of the eye-tracking ratios either (all $P > 0.05$). Nor did we observe significant correlations between the ratios and intellectual functioning (FSIQ, PIQ or VIQ). Finally, no relationship was detected between the ratios and the PSI, or the separate PSI subtests, Symbol

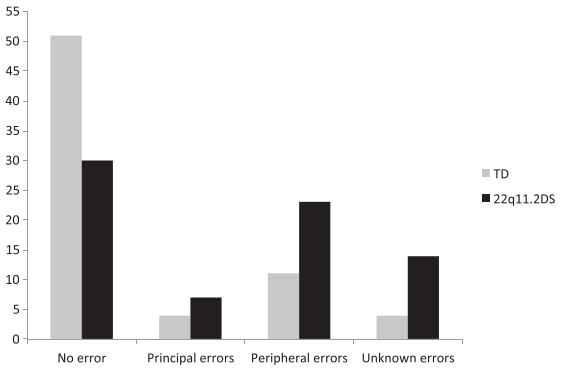

Figure 3 Number of participants with 22q11.2DS and TD individuals who made no error, at least one principal error, at least one peripheral error or unknown errors on the computerised Benton Visual Retention Test.

Search or Coding. Significant correlations were not observed between eye-tracking and memory or executive functioning variables in the TD group (all $P > 0.05$).

As a previous study showed atypical visual exploration during the BVRT in patients with schizophrenia (Obayashi *et al.* 2003), we repeated all of the analyses were repeated without the participants with a comorbid psychotic disorder ($N = 7$). Our results remained unchanged, with the exception that we no longer observed a significant group difference for the average fixation duration ratio ($Mdn_{TD} = 1.08$, $Mdn_{22q11.2DS} = 0.97$, $U = 1914.00$, $z = -1.86$, $P > 0.05$).

Discussion

The current study is the first to investigate visual exploration during a short-term memory recognition task in patients with 22q11.2DS by combining a C-BVRT with eye-tracking technology. This allowed for further investigation of the factors contributing to visual short-term memory impairments in the syndrome.

Individuals with 22q11.2DS showed an atypical exploration pattern compared with TD participants during the encoding of visual stimuli, confirming our first hypothesis. Patients with 22q11.2DS spent more time on the principal regions of interest and neglected the smaller peripheral figures compared with healthy controls. These results are commensurate with previous evidence showing abnormal scanning of visual stimuli in 22q11.2DS (Franchini *et al.* 2016; Campbell *et al.* 2010; McCabe *et al.* 2011; Glaser *et al.* 2010). Additionally, in accordance with the study of McCabe *et al.* (2011), our results provide further evidence that differential visual scanning of individuals with 22q11.2DS is not limited to faces. Importantly, these studies also have shown that abnormal visual exploration may have maladaptive consequences. For example, Glaser *et al.* (2010) suggested that differential exploration of faces may contribute to social difficulties reported in 22q11.2DS, and in the study of McCabe *et al.* (2011), an impoverished scanning strategy was associated with lower accuracy on the weather task.

In the present study, atypical visual exploration resulted in lower performance on a memory task, confirming our second hypothesis. Commensurate with previous reports of reduced mnemonic abilities in the syndrome (Campbell *et al.* 2010; Gur *et al.* 2014; Bostelmann *et al.* 2016), individuals with 22q11.2DS exhibited lower memory scores on the C-BVRT compared with healthy controls. Furthermore, we found that individuals affected by the syndrome with shorter average fixation duration ratios (indicating shorter fixations on the peripheral figures compared with the principal figures) were characterised by poorer accuracy on the C-BVRT. It has been suggested that longer fixations may result in deeper information processing (Loftus 1981). Moreover, multiple and longer fixations help maintain information about the location of target objects within a scene and their specific properties (Tatler *et al.* 2005; Hollingworth & Henderson 2002). In other words, numerous and long fixations on an element promotes better encoding/memory (Saint-Aubin *et al.* 2007; Guerard *et al.* 2009). In our study, it was harder for both groups to recognise peripheral elements compared with principal ones, and as a result, they made more peripheral errors on the task. However, the fact that participants with 22q11.2DS had more trouble exploring all the parts of a stimulus (i.e. peripheral elements) may have contributed to the increase in the number of peripheral errors in the 22q11.2DS group. Contrary to what one might think, increased time spent fixating on a stimulus can be correlated with trouble extracting information (Bojko 2013). This may suggest that the processing of principal figures is more effortful for patients with 22q11.2DS, causing them to neglect other parts of the stimuli.

Our third hypothesis addressed the fact that visual attention may rely on other underlying cognitive abilities, including vigilance, or the ability to orient towards a stimulus and exert executive control (Posner & Petersen 1990). We had postulated that an atypical visual processing pattern in 22q11.2DS may be linked to slow information processing. However, our data showed that although participants with 22q11.2DS had lower PSI scores compared with the control group, none of the eye-tracking parameters were significantly correlated with PSI. Similarly, Bish *et al.* (2005) found no impairment of the attentional alerting and orienting systems in 22q11.2DS. We also expected that individuals' with 22q11.2DS ability to visually explore stimuli during encoding may be hindered by their executive dysfunction. Our data showed that 22q11.2DS participants focused more attention on principal than peripheral figures, suggesting a lack of organisation in their visual exploration of the stimuli. A similar phenomenon was demonstrated in Glaser *et al.* (2010), who observed more diffuse fixations on faces, without a clear, goal-oriented exploration pattern.

We had postulated that a different exploration of the stimuli than observed in the control group could be related to inhibition difficulties in 22q11.2DS. We did not, however, observe a significant relationship between any of our inhibition variables and visual scanning variables. This may be due to an important methodological difference between our study and previous studies. While preceding studies used stimuli presented for very short periods of time in milliseconds (Sobin *et al.* 2004; Simon *et al.* 2005), stimulus presentation in the C-BVRT lasted for 10 full seconds. An alternative explanation for the lack of association between the visual exploration and inhibition data may be due to the specific inhibition task that was used in this study (the CPT). While the CPT is informative for understanding inhibition based on a prepotent visual response, alternative inhibitory control processes may be more related to C-BVRT task demands. One such inhibitory process could be cognitive inflexibility, which is known to be impaired in 22q11.2DS and may well impact visual scanning (Shapiro *et al.* 2014; Woodin *et al.* 2001). Cognitive flexibility is the ability to shift attention from previously relevant stimuli, an effort that depends on both inhibitory control and working memory (Diamond 2013). Impaired cognitive flexibility, or cognitive inflexibility, may result from switching one's attention from one part of a stimulus to another during the C-BVRT, resulting in an excessive focus on the principal figures compared with the peripheral ones. Similarly, Bish *et al.* (2007) showed that 22q11.2DS have trouble managing shifts in spatial attention between four different objects. Difficulty re-engaging with a new target may also explain why participants with 22q11.2DS would have explored the peripheral elements to a lesser extent when they were presented with multiple components to encode (Simon *et al.* 2005; Simon *et al.* 2005). Finally, it has been shown that individuals with 22q11.2DS are impaired at temporal perception (Debbané *et al.* 2005). Participants with 22q11.2DS may have run into trouble managing their time during the encoding phase. Given that spatial orientation depends on a number of cognitive processes, further investigation is clearly needed to better understand the putative impairments affecting memory in 22q11.2DS.

This study is an initial investigation of visual attention during memory encoding in 22q11.2DS. It is useful for identifying cognitive mechanisms that may potentially influence memory impairments; however, is it preliminary and affected by limitations that can inform the experimental designs of future studies. The C-BVRT eye-tracking task was designed in keeping with the description of the original BVRT in the test manual. However, the encoding phase ended up being relatively long (10 s) for an eye-tracking task, and we could not control the use of top-down processes during encoding, such as the implementation of strategies (for instance verbal strategies) during encoding that could influence visual processing of the stimuli (Tatler *et al.* 2005). Second, the C-BVRT was not designed for qualitative analysis of error type because of the relatively small number of items in the test. We went ahead with this part of our analyses because they are descriptively informative, but they also are, without a doubt, statistically limited. It is also worth noting that as part of the same research protocol, all participants completed the paper and pencil version of the BVRT approximately 24 h before the C-BVRT. Given that the two administrations are based on the same stimuli, this could have influenced their exploration of the stimuli during the encoding phase. In the present study, we only tested variables using time (duration)

and number (quantity of fixations). In the future, other eye-tracking variables, including the distance between the fixations, could help to further characterise differential exploration in 22q11.2DS. Finally, while the presence of psychosis in a portion of the patients with 22q11.2DS appeared to have a minor impact on our results, traits related to a high risk for schizophrenia in the syndrome may still have impacted the group's visual exploration during the encoding phase (Sprenger *et al.* 2013; Streit *et al.* 1997). Future studies could examine this potential relationship in a larger group of participants affected by 22q11.2DS and schizophrenia, or by studying the impact of positive or negative symptoms on visual exploration.

In conclusion, this preliminary study suggests that individuals with 22q11.2DS demonstrate atypical exploration while learning visual information and focus their attention on principal elements at the cost of exploring peripheral elements. This study can help us to understand previously reported memory impairments in 22q11.2DS (Campbell *et al.* 2010; Lajiness-O'Neill *et al.* 2005; Bostelmann *et al.* 2016) and clinical observations made by practitioners and educators who work with affected individuals. The present results additionally may help to shed light on effective learning strategies and useful adaptive measures, such as creating visually simple school material and pointing out elements that are located on the perimeter of the page and more easily missed.

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Conflict of Interest

The authors declare that they have no competing interests.

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