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Visual processing of emotional dynamic faces in 22q11.2 deletion syndrome

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Abstract

Introduction The 22q11.2 deletion syndrome (22q11DS) is a neurogenetic syndrome. Individuals affected by this syndrome present poor social functioning and a high risk for the development of psychiatric disorders. Accurate emotion recognition and visual exploration of faces represent important skills for appropriate development of social cognition in individuals with 22q11DS. For these reasons, there is elevated interest in establishing relevant ways to test the mechanisms associated with emotion recognition in patients with 22q11DS.
Methods This study investigated emotional recognition and visual exploration of emotional faces in persons with 22q11DS, with a dynamic emotion task using an eye-tracking device. To our knowledge, no previous studies have used emotional dynamic stimuli with 22q11DS, despite improved ecological validity of dynamic stimuli compared with static images. Furthermore, these stimuli provide the opportunity to collect reaction times, as indicators of the emotional intensity necessary for identifying each emotion.
Results In our task, we observed comparable accuracy in emotion recognition in the 22q11DS and healthy control groups. However, individuals with 22q11DS were slower to recognise the emotions. They also spent less time looking at the nose during happy and fearful faces.
Conclusions These results suggest that individuals with 22q11DS may need either more time or more pronounced emotional cues to correctly label facial expressions.

Keywords eye-tracking, facial emotion recognition, FACSGen, reaction times, 22q11.2 deletion syndrome

Introduction

Identifying emotions efficiently and accurately is essential to establish interpersonal relationships. In some neurogenetic syndromes, such as the 22q11.2 deletion syndrome (22q11DS, also known as velocardiofacial or DiGeorge syndrome), emotion recognition, and thus social functioning, is impaired (Jalbrzikowski *et al.*, 2012). Exploring visual exploration of emotional faces in people affected by this syndrome may help us to understand the

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mechanisms underlying their emotion recognition impairments.

The 22q11DS is a genetic condition affecting approximately 1 in 2000 newborn babies (Shprintzen, 2008). Affected individuals frequently present cardiac malformations and velopharyngeal insufficiency, in addition to a neuropsychiatric profile characterised by lower IQ and high rates of anxiety and mood disorders. Affected individuals also have increased risk for developing schizophrenia (Gothelf *et al.*, 2007). Given these concerns, it is not surprising that poor social skills are also a defining characteristic of children with 22q11DS (Shashi *et al.*, 2012). A growing body of evidence shows that at least part of impaired social functioning in 22q11DS can be explained by deficits in face and emotion recognition. Previous studies have related emotion recognition to psychopathology (e.g. anxiety disorders; Glaser *et al.*, 2010) and decreased social skills (Campbell *et al.*, 2010) in this syndrome. In addition, previous studies have found face perception deficits in people with 22q11DS, a finding that may be syndrome-specific. Campbell *et al.* (2009) showed a specific deficit in children with 22q11DS on a face-matching task compared with children with Williams Syndrome. Other studies suggested that individuals with Williams Syndrome show prolonged face gaze with exaggerate fixations on the eyes, which may also represent an impairment, impacting social-communicative learning in the syndrome (Riby & Hancock, 2008, 2009). A syndrome-specific deficit would point to a specific role for the genes in the deleted 22q11 region in differential processing of social stimuli. Other findings show that children with 22q11DS manifest impairments in face memory and successful face identification (Campbell *et al.*, 2011; Lajiness-O'Neill *et al.*, 2005). These findings are complemented by functional magnetic resonance imaging studies demonstrating abnormal cerebral responses in 22q11DS when processing faces (Andersson *et al.*, 2008; Van Amelsvoort *et al.*, 2006). Structural changes in the fusiform area (a key region for face recognition) have been consistently demonstrated in 22q11DS (Debbané *et al.*, 2006; Deboer *et al.*, 2007; Glaser *et al.*, 2007).

Eye-tracking technology has made it possible to analyze the details of face exploration strategies during emotion recognition tasks. For instance, in a study of emotion recognition in healthy young adults (Schurgin *et al.*, 2014), participants primarily spent more time on salient facial features (eyes, nose and mouth) than on other facial regions. However, the time spent on each of these features differed by the emotion presented: participants spent more time on the mouth when recognising happy faces and more time on the eyes for angry, sad and fearful faces. In another study with healthy adults, Bassili (1979) showed the importance of facial movement during dynamic emotion recognition. For example, mouth movement during a happy expression was a key feature in the correct identification of the expression (Krumhuber *et al.*, 2013).

Several studies have used eye-tracking to study visual exploration of faces in 22q11DS, giving insight into the way affected individuals scan faces. In a previous study, our group found that children and young adolescents with 22q11DS spent more time on the mouth region and less time on the eyes during a static face discrimination task compared with both healthy controls and individuals with developmental delay (Glaser *et al.*, 2010). Moreover, time spent on the eyes was related to both parent-reported and self-reported anxiety and IQ in the 22q11DS group. Campbell *et al.* (2010) showed similar maladaptive strategies in adolescents with 22q11DS during visual scanning of emotional faces. Participants with 22q11DS demonstrated more fixations on the mouth than the eyes and reduced emotion recognition while viewing static pictures of emotional faces (happiness, sadness, surprise, anger, fear, disgust and neutral). This result was strongest for the negative emotions (anger, fear and disgust).

These findings support the idea that investigating visual scanning of faces in 22q11DS may be the key to understanding emotion recognition impairments and social issues in affected individuals. In a past study, we explored visual scanning of faces in individuals with 22q11DS, idiopathic developmental delay and healthy controls (Glaser *et al.*, 2010). Individuals with 22q11DS were more impaired on configural processing of faces than featural processing. Configural processing is essential to emotion recognition (Calder *et al.*, 2000). However, it is important to keep in mind that less specific anomalies in visual exploration have also been detected in the syndrome. For example, McCabe *et al.* (2011) showed several pictures of emotional faces and non-social complex visual scenes to adolescents with

22q11DS. This study showed that visual scanning is not only impaired in pictures of faces but also for complex visual scenes. Further, these patients manifest visuospatial deficits affecting the rapidity with which they recognise features embedded in complex forms (Giersch *et al.*, 2014; Simon *et al.*, 2005) such as scenes and faces. Therefore, a global processing issue in people with 22q11DS may further complicate configural processing of faces, helping to explain emotion recognition impairments in the syndrome.

To our knowledge, no study to date has explored visual scanning of dynamic emotional expressions in 22q11DS despite improved ecological validity of dynamic stimuli compared with static images (Alves, 2013). Results can be quite different between emotion-processing studies using different types of stimuli. For example, in contrast with previous findings using static images of emotional faces, Souto *et al.* (2012) found no differences between a group of adults with schizophrenia and healthy controls on an emotion-recognition task using dynamic stimuli. On the other hand, a study by Speer *et al.* (2007) in autism shows differences between dynamic and static facial processing, with autistic individuals looking less at the eyes during dynamic stimuli. This supports the hypothesis that dynamic and static facial stimuli are processed differently. Furthermore, Kilts *et al.* (2003) found dissociable neural substrates between the recognition of static and dynamic emotional stimuli, suggesting that their processing relies on different neuronal circuits. Dynamic stimuli also offer the advantage of testing varied intensities of an emotion by capturing the evolution of a neutral face into a clearly emotional face. This is important because there is evidence that the intensity of an emotional expression affects recognition accuracy and, therefore, study results. Emotions are typically better recognised at higher intensities. A study by Kohler *et al.* (2003) showed for instance that this is the case for patients with schizophrenia. Individuals with schizophrenia typically perform worse than healthy controls on emotion recognition tasks; however, they were greatly assisted when the intensity of emotional expressions in static photos was increased. Given that 22q11DS has high co-morbidity with schizophrenia and psychotic disorders (Gothelf *et al.*, 2007), exploring emotion recognition in this population is especially pertinent.

In this paper, we explore visual scanning of faces using a dynamic emotion recognition task. Forty-eight short movies of neutral faces that changed from neutral to angry, happy, fearful or sad faces (see Fig. 1 as an example) were presented to participants with 22q11DS and healthy controls. The consideration of disgust and surprise as 'universal emotions' is a topic of debate in the literature (Ekman & Friesen, 1975; Ekman, 1992). However, we decided not to include them in our task based on the idea that they are not discrete emotions but rather hybrids of other emotions (Kohler *et al.*, 2003, p.1769). In addition, for our first study of dynamic emotion recognition, we preferred a task design that allowed us to collect more items representing fewer emotions to be able to clearly differentiate the scanpaths from the included emotions. It is important to notice that, despite the importance of a cross-syndromal approach, the main goal of the present study was not to investigate the 22q11DS rather than syndromal specificity of face processing. For this reason, we decided to compare 22q11DS with a healthy control group.

Participants were asked to press the space bar and name the emotion as soon as they recognised it. These reaction times were recorded as indicators of the emotional intensity necessary to identify each emotion. A common problem facing researchers studying abnormal development is how to compare two groups with inherent IQ differences, such as 22q11DS and healthy controls. For this reason, we expressly designed this emotion-recognition task so that individuals with 22q11DS could perform similarly to controls, which allowed us to compare visual scanning of emotions in two groups who both performed well on the task. We expected that the ecological validity of our stimuli would enable participants with 22q11DS to perform well on the task, as was shown by Souto *et al.* (2012) in patients with schizophrenia. Moreover, per Kohler *et al.* (2003), we expected individuals with 22q11DS to recognise emotions when they were further on in the dynamic films and the faces presented were higher in intensity with more exaggerated expressions. Accordingly, we expected longer reaction times in the 22q11DS group compared with the control group. We also expected to observe less efficient scanning strategies in the 22q11DS group (less time spent on

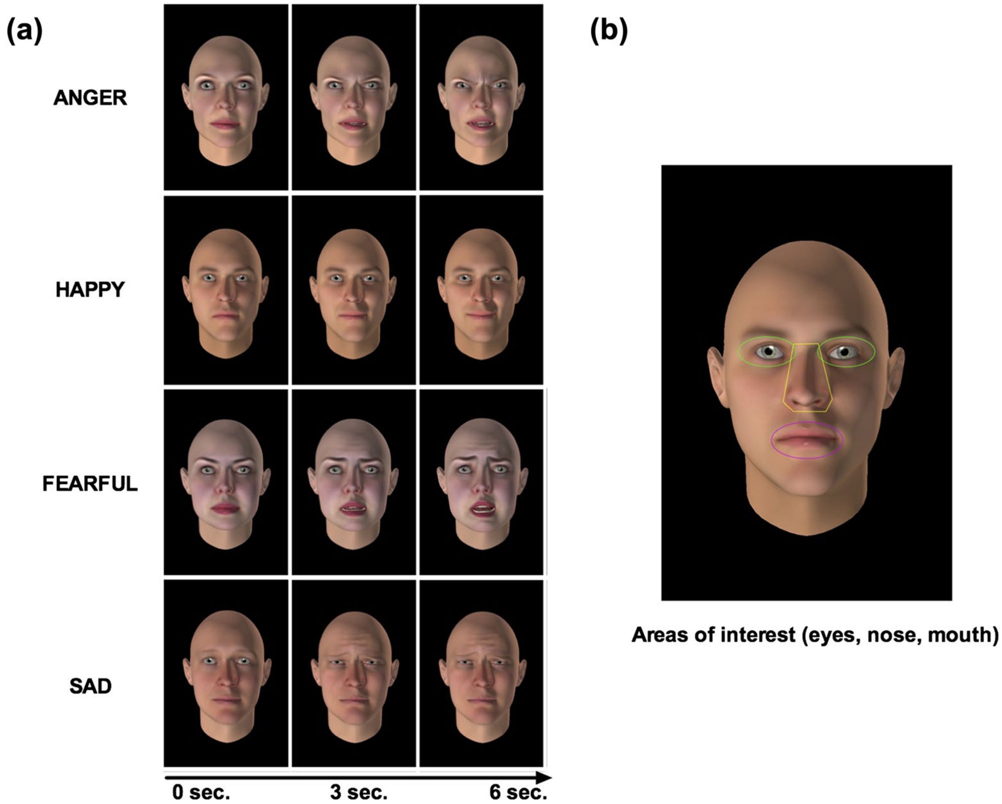

Figure 1 (a) Still shots of four stimuli at 0, 3 and 6 s. (b) Visual representation of the regions of interest used to analyze participants' visual exploration patterns.

features that are salient for emotion recognition) according to previous eye-tracking studies in the syndrome (Campbell *et al.*, 2010; Glaser *et al.*, 2010; McCabe *et al.*, 2011).

Method

Participants

A total of 35 participants with 22q11DS took part in the study [24 females, 11 males; aged 9 to 33 years, $m = 18.2$ (SD = 5.9)]. Four additional participants (3 females, 1 male) participated in the protocol but were not included in the analyses because they did not reach 80% accuracy on the dynamic emotion task. We included only those who had a good accuracy on the task in order to adequately compare the two groups. Mean full-scale IQ for the included participants was 69.5 (SD = 11.3), and the mean processing speed index score was 83.8 (SD = 2.6). In participants under 17 years old, IQ was measured using the Wechsler Intelligence Scale for Children, Third Edition (Wechsler, 1991). In participants from 17 years old, IQ was measured with the Wechsler Adult Intelligence Scale-III (Wechsler, 1997).

Participants were recruited through French-speaking parent associations and were tested in our research laboratory during an ongoing longitudinal study. All persons or their parents (if minors) gave their informed consent prior to their inclusion in the study. Some participants had one or more psychiatric diagnoses at the time of the testing: two individuals had psychosis, one had subclinical psychosis, three had attention deficit disorders, five anxiety disorder, four major depressive disorder, and five obsessive–compulsive disorder. Psychotic symptoms of some kind, either hallucinations or delusions, were detected in 35.9% of the sample (14 in 39 participants). These percentages are consistent with previous studies (Gothelf *et al.*, 2013; Debbané *et al.*, 2006).

Thirty-one typically developing individuals (17 males, 14 females; aged 8 to 31 years, $m = 17.1$, $SD = 6.2$) participated in the study. Individuals were recruited through public schools and announcements in the Geneva community or were siblings of the 22q11DS patients. Potential participants were first screened for neurological/psychiatric problems and learning disabilities through an interview over the phone and completed a medical developmental history questionnaire completed before their visit. This structured interview includes questions about participants' current and past medical and psychiatric history. The controls were group-matched for age with the 22q11DS group. They all met the inclusion criteria of at least 80% accuracy on the dynamic emotion task. Mean full-scale IQ for the control group was 107.6 ($SD = 11.3$), and mean processing speed index score was 105.3 ($SD = 2.9$). We did not detect differences in age between the groups ($p = 0.86$); however, we did detect differences in IQ ($P < 0.001$) and processing speed ($P < 0.001$). As in patients with 22q11DS, IQ was measured with the Wechsler Intelligence Scale for Children, Third Edition (Wechsler, 1991) and the Wechsler Adult Intelligence Scale-III (Wechsler, 1997). The groups also performed differently on the Benton Facial Recognition Test (BFRT, Benton *et al.*, 1994), $F = 28.15$, $P < 0.01$, $df = 1$. The average score was 37.78 ($SD = 1.07$) in the 22q11DS group and 44.96 ($SD = 1.74$) in the control group. Although it approached significance, the gender distribution was not statistically different between the two groups ($P = 0.08$).

Assessment instruments

The dynamic emotion task

The dynamic emotion task (DET) is a dynamic facial task for the assessment of emotion recognition. The stimuli were created using FACSGen 2.0, a software developed by the Swiss Center for Affective Sciences at the University of Geneva, Switzerland (Krumhuber *et al.*, 2010; Mumenthaler & Sander, 2015; Roesch *et al.*, 2011). FACSGen is a relatively recent tool for the creation of realistic artificial facial stimuli based on the Facial Action Coding System method (Krumhuber *et al.*, 2010), a method that describes the facial muscular movements involved in facial expressions. Our stimuli consist of 48 dynamic videos of faces during 6 s each. The videos expressed one of four emotions (12 videos for each emotion): anger, fear, happiness, or sadness. For each emotion, six videos depicted female faces and six were male. The videos all begin with a neutral expression and progressively grow into an emotion, with the emotion becoming gradually more intense and clearly expressed (Fig. 1).

The task was programmed and administered using Tobii Studio software (www.tobii.com) and was implemented on a T60XL eye-tracker with a 17-inch display with a maximum resolution of 1920 × 1200 pixels and a sampling rate of 60 Hz. The Tobii machine can tolerate moderate head movement at 60 cm in front of the device, which is why participants were positioned approximately 60 cm away from the screen. During the task, fixation points were calculated when gaze points lasted at least 100 ms and fell within a circle encompassing 30 pixels. Following data collection, regions of interests (ROIs) were drawn (Fig. 1) on the videos to delineate the eyes, nose and mouth and to calculate the time spent in these specific areas (the totality of fixation duration).

Procedure

Before administering the task, all participants completed a five-point calibration procedure to detect eye motion and eye gaze. The procedure consisted of following a red dot on a light-coloured screen with both eyes. Calibration was repeated until each participant hit all five of the points with both eyes. Participants were then given a standard set of instructions before the task:You will see some short

> films of faces. Each face expresses one emotion. Please tell me the emotion that is being expressed in each film. The faces may be angry, happy, fearful, or sad.The four emotions were written on a paper sheet and placed under the screen where the participants could refer to them. Participants were also instructed to press the space bar as soon as they recognised the emotion and to name the expression to the examiner. The videos remained on the screen until the participant pressed and gave an answer (if they answered during the video) or until the end of the video in the absence of any press by the participant (each video had a duration of 6 s). Four practice trials were presented and discussed aloud to confirm the participant's understanding of the

task. All participants showed sufficient understanding of the task by the end of the instructions and practice trials. A white fixation cross appeared in the centre of the screen for 2 s between each stimulus, and participants were told to keep their eyes on the fixation cross until the face appeared. The videos were presented in a fixed randomised order and the examiner recorded the participants' responses.

The Benton Facial Recognition Test

The BFRT (Benton *et al.*, 1994) is a standardised measure of face recognition. The long form consists of 22 target faces and 54 items in which the participant must identify one to three black and white photos of a target person, despite variable changes in orientation and lighting. An 'average' score ranges from 41–54. The 'moderate to borderline' range is between 37 and 40, and scores below 37 correspond to a 'severe' deficit in face recognition.

Data analysis

We started by examining each participant's data on the DET to verify that the subjects understood the task and determine that each participant had reached at least 80% accuracy on the task (combined trials). Visual exploration on the DET was subsequently examined. The time spent in a specific ROI was calculated by the percentages of fixation duration on each feature (eyes, nose and mouth) and on the three features combined. Percentages were calculated by dividing fixation duration on each feature by total fixation duration from each stimulus. Group distributions were then checked for normality and heterogeneity of variance for two variables: reaction time and percentage of time spent on facial features. Descriptive data (mean and SD) are listed in Tables 1 and 2. Multivariate analysis of variance or Mann–Whitney tests were run in SPSS Statistics 22.0 for Mac with diagnosis as a fixed variable. Gender, age and IQ were controlled for each analysis: no main effect of these variables was found. We then correlated reaction time and processing speed index score. Next, we tested for relationships between other cognitive measures (BFRT and IQ) and performance on the DET (time spent on features and reaction times) using correlation analyses. Results were considered significant at $p < 0.05$.

Results

Accuracy

The 22q11DS and control groups demonstrated comparable performances on the DET: mean accuracy was 93.70% (SD = 22%) in the 22q11DS group and 94.44% (SD = 3.58%) in the control group ($F = 0.054$, $P = 0.81$, df = 1).

Reaction Times

The 22q11DS group responded on average in 4.38 s (SD = 0.60) and the control group in 3.91 s (SD = 0.68), which are statistically different ($F = 3.45$, $P < 0.01$, df = 1). Individuals with 22q11DS answered later in the stimuli and thus recognised the emotions when the expressions were more exaggerated or intense. This was the case across all four emotions

Table 1 Mean (SD) reaction times (in seconds) by emotion for each group and the percentage (SD) of occurrences when a group stopped the stimulus by pressing before the end of the film

	Reaction times (seconds)			Bar press (%)		
	22q11DS (n = 35)	Controls (n = 31)	Significance (MANCOVA)	22q11DS (n = 35)	Controls (n = 31)	Significance (Mann–Whitney)
All emotions	**4.38 (0.60)**	**3.91 (0.68)**	**$F = 3.45$, $P < 0.01$***	**82.62 (19.28)**	**92.00 (8.64)**	**$U = 337.5$, $P < 0.01$****
Anger	4.22 (0.71)	3.77 (0.82)	$F = 7.50$, $P < 0.05$*	86.19 (21.29)	96.51 (7.99)	$U = 367.0$, $P = 0.01$**
Happiness	4.10 (0.69)	3.45 (0.76)	$F = 10.51$, $P < 0.001$***	89.76 (20.02)	97.58 (5.77)	$U = 378.0$, $P < 0.05$*
Fear	4.40 (0.83)	4.04 (0.84)	$F = 2.26$, $P = 0.074$	81.90 (23.18)	89.78 (12.49)	$U = 432.5$, $P = 0.14$
Sadness	4.8 (0.54)	4.4 (0.69)	$F = 7.61$, $P < 0.05$*	72.62 (23.62)	84.14 (19.05)	$U = 353.5$, $P < 0.05$*

Table 2 Regions of interest: mean (SD) percentage of time spent on features (eyes, nose and mouth) relative to time spent on the head.

	Fixations on features (%)			Fixations on eyes (%)			Fixations on nose (%)			Fixations on mouth (%)		
	22q11DS (n = 35)	Controls (n = 31)	Significance (Mann–Whitney)	22q11DS (n = 35)	Controls (n = 31)	Significance (Mann–Whitney)	22q11DS (n = 35)	Controls (n = 31)	Significance (Mann–Whitney)	22q11DS (n = 35)	Controls (n = 31)	Significance (Mann–Whitney)
All emotions	**59 (25.52)**	**70.73 (20.44)**	**U = 408.0, P = 0.071**	**15.99 (16.42)**	**18.50 (13.84)**	**U = 477.0, P = 0.16**	**19.52 (10.90)**	**28.52 (16.96)**	**U = 390.5 P = 0.05**	**23.70 (15.29)**	**23.97 (17.09)**	**U = 540.0, P = 0.97**
Anger	58.77 (26.03)	71.05 (22.69)	U = 400.0, P = 0.065	15.75 (18.48)	17.99 (14.73)	U = 422.0, P = 0.12	23.00 (12.33)	30.79 (18.46)	U = 416.0, P = 0.10	22.27 (14.90)	20.84 (16.48)	U = 498.5, P = 0.57
Happiness	61.01 (27.51)	71.09 (23.61)	U = 437.0, P = 0.15	10.95 (12.73)	13.12 (11.19)	U = 416.0, P = 0.10	16.89 (11.71)	24.29 (12.94)	U = 354.5, $P < 0.05$*	33.68 (21.06)	33.70 (23.25)	U = 883.0, P = 0.88
Fear	60.02 (26.75)	75.06 (18.99)	U = 378.0, $P < 0.05$*	15.46 (16.41)	16.18 (13.47)	U = 467.0, P = 0.33	18.97 (11.94)	30.32 (19.08)	U = 345.5, $P < 0.05$*	28.56 (18.34)	26.31 (19.72)	U = 498.50 P = 0.57
Sadness	56.89 (25.74)	67.31 (22.53)	U = 417.0, P = 0.11	21.03 (20.98)	24.72 (19.70)	U = 469.0, P = 0.36	18.86 (12.41)	28.28 (20.13)	U = 439.0, P = 0.18	14.31 (12.47)	16.89 (14.44)	U = 581.5, P = 0.62

combined, as well as for three separate emotions (anger, happiness and sadness) but not for fear (Table 1). Slower reaction times in the 22q11DS group can partially be explained by the fact that individuals with 22q11DS pressed the space bar (to stop the stimulus and respond) less frequently than controls and thus were often exposed to the highest intensity level for each expression at the end of each stimulus. In fact, across emotions, individuals with 22q11DS pressed the bar for 82.62% (SD = 19.28) of the items and the control group for 92.00% (SD = 8.64), which are statistically different (U = 337.5, P < 0.01, df = 1). Similar to reaction time, this held true for anger, happiness and sadness but not for fear (Table 1). Accordingly, individuals with 22q11DS gave their answers at the end of the film more often than controls. We did not observe a correlation between reaction time on the DET in the 22q11DS group and processing speed (r = −0.02, P = 0.92).

Visual exploration of the stimuli

We first checked for potential differences in the totality of time spent on the screen between the control and 22q11DS groups (t = 0.19, P = 0.8521, df = 1). When comparing time spent on the combined features (eyes, nose and mouth), we observed trend-level significance for all the emotions combined. For fearful faces only, the 22q11DS group looked significantly less at the combined facial features compared with the control group (U = 378.0, P < 0.05, df = 1). For the separate facial features, the 22q11DS group looked significantly less at the nose (compared with the control group) for all the emotions combined. When analyzing the emotions separately, this result is significant for happy and fearful faces. We did not observe between-group differences for time spent on the eyes and mouth (Table 2). Fig. 2a shows the gaze patterns (i.e. time spent on each feature during the films) by group for each emotion. The gaze patterns of the two groups are strikingly similar (Fig. 2b).

The time spent on the combined features (i.e. eyes, nose and mouth together) correlated with accuracy on the BFRT in 22q11DS (r = 0.42, P < 0.05, Fig. 3) but not controls (r = −0.21, P = 0.25). We did not find any correlation between the age and the performance in the DET, if considering all the three features together. However, we found a trend for a negative correlation between the age and the time spent on the eyes in the control group (r = −0.32, P = 0.08). Additionally, we observed a trend for a positive correlation between age and time spent on the mouth in the 22q11DS group (r = 0.32, P = 0.06). We did not observe any relationship between IQ and performance in the DET for the 22q11DS (r = 0.15, P = 0.39) or control (r = −0.11, P = 0.56) groups. We also did not observe any relationship between IQ and performance in the DET for the 22q11DS (r = 0.15, P = 0.39) or control (r = −0.11, P = 0.56) groups.

Discussion

In the current study, we used dynamic stimuli created with the FACSGen program (Roesch *et al.*, 2011) to investigate emotion recognition in patients with 22q11DS and healthy controls. The DET offered a rare window of opportunity to analyze a task on which individuals with the syndrome performed comparably with controls. We found that participants with 22q11DS recognised emotional expressions later in the dynamic films and spent less time gazing at the facial features of the faces, with significant differences in time spent looking at the nose region compared with healthy controls during happy and fearful faces. However, their exploration patterns over the 6-s films were remarkably similar, although slightly delayed, compared with controls. Time spent on the features was correlated with facial recognition scores from the BFRT (Benton *et al.*, 1994) in the 22q11DS group. Taken together, these results point to differential processing of dynamic emotional faces in 22q11DS compared with previous studies using static faces.

The fact that our participant groups demonstrated comparable accuracy on the emotion recognition task allowed us to compare reaction times and visual exploration patterns between groups without the additional concern of whether the 22q11DS participants understood the task. Our 22q11DS group was slower to recognise emotions, suggesting that they may need either more time, or more exaggerated and intense emotions, to correctly label facial expressions. This observation supports the idea that processing speed may be central to efficient emotion recognition in 22q11DS, a conclusion that has been drawn from working with healthy adults on computerised visuospatial tasks (De Sonneville *et al.*, 2002). However, the importance of an accurate

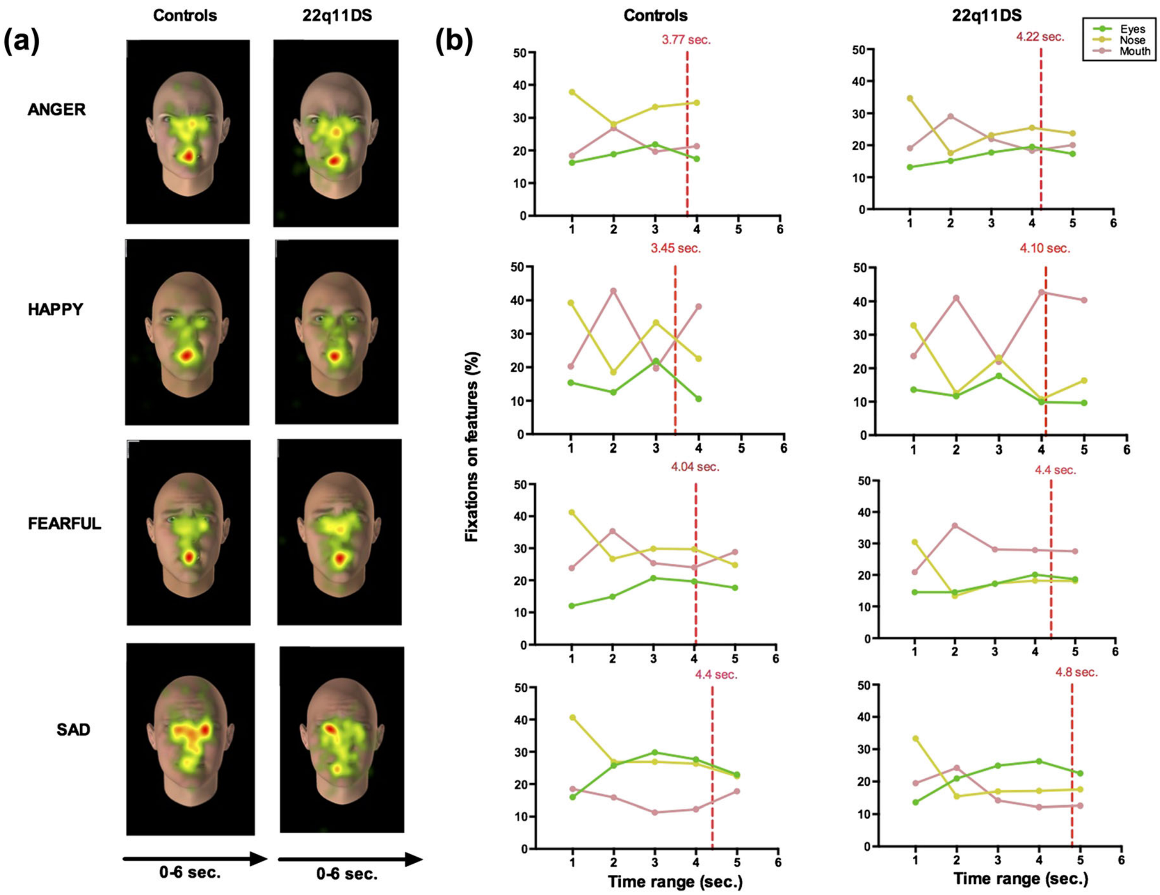

Figure 2 (a) Gaze patterns on heat maps (i.e. colour-coded graphical representations of gaze fixations) represent where participants looked during the 6-s movies for each emotion. Green represents fewer fixations (less time), and red represents more a greater density of fixations. (b) Percentages of time spent on the eyes, nose and mouth during the 6-s movies. Dotted red vertical lines represent mean emotion recognition time (reaction time).

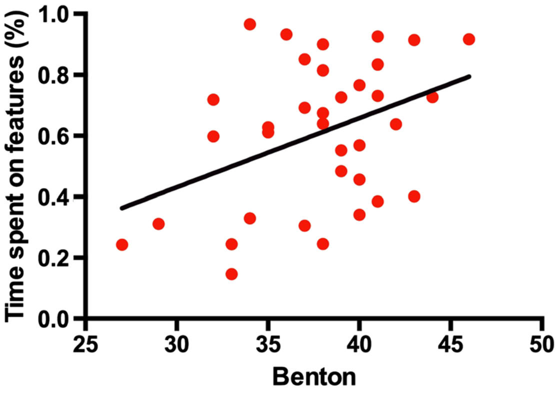

Figure 3 Correlation between total score on the Benton Facial Recognition Test and percentage of time spent on the combined features during the dynamic emotion task in the 22q11DS group.

scanning of faces for proper emotion recognition has been supported by previous studies in other developmental disorders such autism or fragile X (Sawyer *et al.,* 2012; Crawford *et al.,* 2015). Efficient and rapid identification of emotions is essential for active participation in social exchanges. It follows that either poor or slow recognition of subtle emotions could be detrimental to social skills, observations that have been noted in both 22q11DS (Shashi *et al.,* 2012) and schizophrenia (Mueser *et al.,* 1996). Impaired social skills as a consequence of slower emotion recognition may be an additional cause of increased psychopathology, such as anxiety disorders (Shashi *et al.,* 2012), in individuals with 22q11DS. Nevertheless, in our sample, we did not observe a relationship between processing speed and reaction time on the DET in the 22q11DS group. This may be due to the fact that the processing speed index score from the Wechsler IQ scales is general and not specific to visuospatial processing, and because it does not produce precise measures of reaction time like a computerised task.

Analysis of participants' visual exploration patterns showed that the 22q11DS group looked less at the main facial features (eyes, nose and mouth together) than healthy controls. However, when we compared the timing of both groups' visual exploration patterns, they showed many similarities (Fig. 2b). This similarity contrasts with previous studies, which demonstrate reduced time spent on the eyes during neutral and emotional face exploration (Campbell *et al.,* 2010) and comparable time spent on the features of the face between 22q11DS and comparison groups (Glaser *et al.,* 2010). The dynamic stimuli used in our study may partly explain the differences between our results and previous studies using static pictures. For instance, the movement of the mouth is more prominent in dynamic stimuli (Fig. 1) and may have driven both groups' attention away from the eyes towards the mouth. It is also important to remember that our sample includes individuals with 22q11DS who performed comparably with the control group on the task, which may also explain the groups' similar patterns of visual exploration. Indeed, it is possible that we would have observed greater differences in the groups' visual exploration patterns if we had used a dynamic emotion task that discriminated between accuracy performances.

Our results suggest that the main group differences in exploration of the facial features fall on the nose. It is important to keep in mind that the upper part of the nose was considered as a portion of the eye region in previous studies (Glaser *et al.,* 2010; Campbell *et al.,* 2010). Moreover, our result showed a tendency to reduced time spent on the eyes with age in the control group and to increased time spent on the mouth in the 22q11DS group. Thus, age might represent an important point to consider for future works in this field, in order to specify the dynamic of the relationship between age and visual processing of faces. In the current work, time spent on the nose in individuals with 22q11DS was significantly reduced for happiness and fear but not for anger and sadness. Work by Schurgin *et al.* (2014) has shown that healthy adults often reference the eyes to recognise fear and the mouth to recognise happiness. Furthermore, mouth movement is critical to recognising happiness in dynamic facial stimuli (Krumhuber *et al.,* 2013). Reduced time spent on the nose of happy faces in 22q11DS might be explained by reduced time spent on the upper part of the face. It is possible that noticeable movement of the mouth brings participants' gaze to the lower part of the face. However, this consideration would not explain a reduction in time spent on the nose during fearful faces, especially considering that FACSGen fearful faces show obvious movement in both the eye and mouth areas (Kohler *et al.,* 2004). Several studies demonstrating difficulties in emotion recognition in adults with schizophrenia show pronounced difficulty in recognising fearful faces (Kohler *et al.,* 2003; Morris *et al.,* 2009). Likewise, scanning of fearful faces may be particularly impaired in individuals with 22q11DS.

The relationship between intellectual functioning and visual scanning of faces is another important element to consider in the context of 22q11DS, a syndrome associated with cognitive impairment. We did not detect a relationship between IQ and visual scanning of faces in 22q11DS. This differs from results from a previous study pointing to a positive relationship between IQ and time spent on the eyes in participants with 22q11DS (Glaser *et al.,* 2010). It may be that the task employed in the current study facilitated face exploration in our participants, even lower-functioning individuals. Specifically, the eyes may have been more salient in the current study given that the stimuli were dynamic. Alternatively, discriminating between two faces on the screen in the previous study may have introduced an element of complex reasoning or difficult visual exploration that was simplified in this study, which used a single face displayed centrally without other distractions. Finally, it is important to remember that we observed a tendency difference on the time spent on features (eyes and mouth) in relationship with age. This suggests that age plays an important role in the relationship between visual scanning of face and cognitive functioning of individuals with 22q11DS. The latter echoes educational recommendations in the syndrome to simplify the presentation of visual material in order to remove unnecessary distractions (Cutler-Landsman, 2012) and implies that individuals with the syndrome may find dynamic stimuli more accessible than static stimuli in socio-emotional intervention programmes.

In the current study, we also observed a significant correlation in the 22q11DS group only between time spent on facial features and score on the BFRT, a standardised measure of face recognition. Accordingly, individuals with the syndrome who spent more time on the core internal features of a face (the meaningful regions) for emotion recognition were also better at recognising the identity of a face amidst angle and lighting changes. One explanation for this could be due to similarities between the tasks. For example, it may be that dynamic motion isolates certain parts of the face, thereby accentuating changes in expressions and guiding where subjects should look during the DET. The participants who pick up on those details also may be more attuned to the slight visible changes that differentiate the pictures in the BFRT task. This correlation, together with the aforementioned results on the DET, implies pronounced heterogeneity for face identification and emotion processing in the 22q11DS population. Individuals who focus less on the core features of the face may also experience increased difficulty in both face identification and emotion processing. Conversely, the fact that the control group spent sufficient time on the facial features and responded rapidly to the stimuli may be related to their good performance on the BFRT. It is important, however, to keep in mind that the BFRT uses static images of faces. An impairment on the BFRT may be accentuated by a general problem processing static images of faces in 22q11DS, an idea that is commensurate with results from several eye-tracking studies in the field (Campbell *et al.,* 2010; Glaser *et al.,* 2010; McCabe *et al.,* 2011).

There are methodological limitations that should be taken into account when interpreting the findings from the current study. First, due to technical constraints for drawing dynamic ROI, the ROI that we used on the nose region of our stimuli encapsulated the entire nose region, including the upper part between the eyes. This is in contrast with the ROIs used by Glaser *et al.* (Glaser *et al.,* 2010) for which the upper part of the nose was counted as part of the eyes region. We did not find precise information explaining how the regions of interest were defined in the other study. This methodological difference may have contributed to differences between study results (Glaser *et al.,* 2010 found reduced fixations on the eyes compared with controls, whereas we did not). ROI borders should be more consistent across studies to simplify the comparison between studies. Second, to increase our sample size, the age range of our participants spanned childhood, adolescence and adulthood. However, we were still unable to compare participant sub-groups by age, which would have been informative to our understanding of the developmental trajectory of emotion processing in the syndrome. Future studies may want to restrict the age ranges of the participants to pursue similar questions by developmental period. Third, some of the participants with 22q11DS had other psychological disorders. Previous studies report an influence of psychiatric disorders on emotional face processing (Surcinelli *et al.,* 2006; Easter *et al.,* 2005). Our sample size did not permit us to analyze our results according to the most common psychiatric disorders found in 22q11DS; however, it will be important to address the putative contributions of 22q11DS and psychiatric disorder on face exploration in future studies. Finally, given that speed and accuracy influence emotional face processing in the 22q11DS group, a more precise and timed measure of visuospatial processing speed should be added to future protocols (De Sonneville *et al.,* 2002).

In conclusion, our results suggest that focusing on the visual scanning of emotional faces rather than on accuracy can help us understand the issues underlying emotion recognition in individuals with 22q11DS. Specifically, our findings support the idea that dynamic emotional faces are processed more slowly in individuals with 22q11DS, compared with a healthy control group. Moreover, our results suggest that both processing speed and face identification should be considered when evaluating emotion processing in 22q11DS. Our results support previous studies showing that time spent on the facial features is important for identifying difficulties with individual emotions. Individuals with 22q11DS demonstrated differences in the visual exploration of happy and fearful faces, and featural scanning of faces could depend on age. These findings are critical for effectively designing socio-emotional enrichment materials for individuals with 22q11DS, such as cognitive remediation programmes. Furthermore, identifying individual aberrancies in visual exploration as early as possible may also prove to be critical in improving facial emotion recognition and, consequently, social skills.

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Conflict of Interest

The authors declare no conflict of interest.

Ethical Standards Statement

The local ethical commission of Geneva approved this study.

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