Eur Child Adolesc Psychiatry (2016) 25:297–310
DOI 10.1007/s00787-015-0741-1

ORIGINAL CONTRIBUTION

Facial emotion perception by intensity in children and adolescents with 22q11.2 deletion syndrome

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Received: 24 September 2014 / Accepted: 25 June 2015 / Published online: 7 July 2015

Abstract Difficulties in the recognition of emotions in expressive faces have been reported in people with 22q11.2 deletion syndrome (22q11.2DS). However, while low-intensity expressive faces are frequent in everyday life, nothing is known about their ability to perceive facial emotions depending on the intensity of expression. Through a visual matching task, children and adolescents with 22q11.2DS as well as gender- and age-matched healthy participants were asked to categorise the emotion of a target face among six possible expressions. Static pictures of morphs between neutrality and expressions were used to parametrically manipulate the intensity of the target face. In comparison to healthy controls, results showed higher perception thresholds (i.e. a more intense expression is needed to perceive the emotion) and lower accuracy for the most expressive faces indicating reduced categorisation abilities in the 22q11.2DS group. The number of intrusions (i.e. each time an emotion is perceived as another one) and a more gradual perception performance indicated smooth boundaries between emotional categories. Correlational analyses with neuropsychological and clinical measures suggested that reduced visual skills may be associated with impaired categorisation of facial emotions. Overall, the present study indicates greater difficulties for children and adolescents with 22q11.2DS to perceive an emotion in low-intensity expressive faces. This disability is subtended by emotional categories that are not sharply organised. It also suggests that these difficulties may be associated with impaired visual cognition, a hallmark of the cognitive deficits observed in the syndrome. These data yield promising tracks for future experimental and clinical investigations.

Keywords 22q11.2 deletion syndrome · Social cognition · Emotional expression of faces · Low-intensity expressive faces · Visual skills

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Introduction

The 22q11.2 deletion syndrome (22q11.2DS) is one of the most common microdeletion disorders, with an estimated prevalence between 1 per 2000 and 1 per 6000 depending on the employed method [1, 2]. 22q11.2DS is associated with a large physical phenotypic spectrum, especially congenital heart disease, velopharyngeal problems, and facial dysmorphic features [e.g. 3]. At a neuroanatomical level,

a general reduction of the brain size [4, 5] as well as disorganised white matter tracts [5, 6] have been described. Numerous structural alterations have been detailed in sparse cortical and subcortical areas [5, 7–17].

Moreover, 22q11.2DS is associated with deteriorated socio-emotional behaviour, characterised by withdrawal, shyness, mood problems, and difficulties in the expression of emotions [18–22]. As early as childhood, people with 22q11.2DS are described as having difficulties in initiating and maintaining peer relationships [e.g. 23]. This lack of social skills has been linked to a psychiatric phenotype including increased attention deficits/hyperactivity disorder (ADHD), anxiety and depression [19, 24–30]. It is further estimated that autism spectrum disorders (ASD) occur in 20–50 % of children with 22q11.2DS [24, 31–33]. Besides, a high incidence of psychosis and positive symptoms is observed in patients with 22q11.2DS [34–38]. These symptoms are correlated with their poor social functioning [35, 39] and their anxious and depressive symptoms [40]. Negative symptoms are also frequent in 22q11.2DS with more than 80 % of teenage or young patients presenting with at least one symptom of moderate to severe intensity [41, 42]. These symptoms are good predictors for adaptive abilities [42]. Accordingly, 22q11.2DS is one of the highest known genetic risk factors for schizophrenia [43, 44], accounting for up to 1–2 % of cases in the general population [45, 46] and with approximately 30 % of patients developing schizophrenia in adolescence or early adulthood [34, 37, 40, 47, 48].

22q11.2DS individuals also present with cognitive impairments in executive functioning, memory, and attention [49–51]. Intellectual disabilities are also reported with below-average full-scale IQ [23, 52, 53]. The verbal IQ declines in correlation with the development of psychosis [27, 40], but verbal IQ scores are often higher than performance IQ scores in children with 22q11.2DS [52, 54, 55]. Indeed, poor accuracy in arithmetic and visuospatial processing has been routinely reported in 22q11.2DS [54–57], probably related to structural and functional abnormalities in the parietal lobe [4, 6, 16, 50, 58–61]. Disturbed exploration strategies for complex visual scenes [62] as well as impairments in perceptual categorisation have also been detailed [49]. As a consequence, impaired visual cognition as opposed to relatively "spared" verbal skills seems to be the main characteristic of the neurocognitive deficits found in 22q11.2DS.

Social cognition is a psychological construct referring to the understanding of others' thoughts and including several components such as empathy, theory of mind and emotion processing. Impairments in this field may largely underlie social problems and reduce adaptive skills in 22q11.2DS. Hence, research has recently focused on face processing due to the high relevance of these visual stimuli conveying information about others' mental states. Children with 22q11.2DS suffer from impairments in face memory [50] and have more difficulties than healthy control participants for matching face identity, expression and gaze direction [63]. Besides, adolescents with 22q11.2DS find difficult to label the emotions expressed by faces, especially anger, disgust and fear [62, 64, 65]. Abnormal visual exploration of facial information has been found in 22q11.2DS using eye-tracking techniques [62, 64–66]. These behavioural disabilities may have neural underpinnings in the face-processing network [67], disturbed at both structural [7, 12, 58, 68] and functional levels [61, 69, 70] in individuals with 22q11.2DS.

Although disturbed facial emotion recognition has been repeatedly reported in people with 22q11.2DS, nothing is known about their ability to perceive and recognise facial emotion categories depending on the intensity of expression. Yet, low-intensity facial expressions are frequent in everyday life. Thus, we question the fact that difficulties in individuals with 22q11.2DS may arise because emotional faces must be highly expressive for an accurate categorisation. Accordingly, the present study used static pictures of morphs varying between neutral and expressive faces in order to create a linear increase in the intensity of expression. The aim was to examine whether the intensity needed to accurately recognise facial emotions is higher in young people with 22q11.2DS than in healthy age-matched controls. Moreover, it has been suggested that facial emotions are categorised as discrete entities with clear-cut boundaries [e.g. 71]. In healthy people, this organisation is supported by empirical evidence using morphing techniques and showing an abrupt and non-linear change of perception when varying between two distinct emotions [72–74]. In this respect, the present study further aimed at investigating whether the perception of emotional expressions in 22q11.2DS may be less sharply defined. Precisely, in comparison to healthy participants, we attempted to highlight smoother boundaries between the emotional categories in individuals with 22q11.2DS by showing greater confusions between the expressions and a more gradual perception as the intensity of expression increases. To this end, intrusions (i.e. each time an emotion is perceived as another one) and a sharpness index were, respectively, calculated.

Another purpose of the present study was to explore the cognitive and/or emotional mechanisms that may underlie the difficulties of facial expression recognition in 22q11.2DS. It has recently been shown that people with 22q11.2DS who suffer from predominant negative symptoms are more impaired for the memory of faces than for the memory of verbal information [75]. Likewise, negative symptoms are associated with attenuated social cognitive skills in schizophrenia, especially emotional face processing [76, 77]. In the present study, we computed correlation

scores between behavioural indices of emotion recognition and clinical measures of symptomatology. This was carried out in order to examine whether negative symptoms may be associated with the difficulties of people with 22q11.2DS for categorising facial expressions. It has also been argued that deficits in visual functioning may explain the social difficulties in 22q11.2DS [52]. Accordingly, one may suggest that the deterioration of certain visual skills observed in 22q11.2DS is an important but neglected factor explaining their difficulties in emotional face perception. To evaluate this hypothesis, we also computed correlations between several neuropsychological measures and the behavioural indices recorded in the emotion recognition task. It is to be noted that classic evaluation of emotion recognition is performed using tasks where emotions need to be labelled. This can promote the help of verbal skills. In an effort to minimise the influence of verbal abilities in the present study, we designed a visual matching task that did not require any explicit labelling.

Methods

Participants

Fifteen children and adolescents with 22q11.2DS (5 females, mean age: 14.67 ± 3.13 (SD) years, range 9–19 years) and fifteen healthy participants (5 females, mean age: 14.73 ± 3.01 years, range 9–19 years) were included in the study. The two groups did not differ according to gender (same ratio) and age ($t(28) = 0.06$, $p = .95$). All participants with 22q11.2DS were recruited at Le Vinatier Psychiatric Hospital in Lyon, France. Their diagnosis was confirmed by fluorescence in situ hybridization analysis (FISH). Two of them presented concomitant diagnosis of early onset schizophrenia (DSM-5 criteria), they were treated by antipsychotic medication (olanzapine: 7.5 mg/day and aripiprazole: 10 mg/day) and were clinically stable at testing time. Exclusion criteria were substance abuse, neurological illness, or a history of head injury. Healthy controls were recruited from the community and no history of mental health problems, head injury, or neurological disorder was reported. All participants presented normal or corrected-to-normal visual acuity. The study was approved by the local ethics committee and has therefore been performed in accordance with the ethical standards stated in the Declaration of Helsinki. Parental written informed consent to take part in the study was received for all participants.

Clinical and neuropsychological assessments

Ratings for positive and negative symptoms in participants with 22q11.2DS were obtained using the Positive And Negative Symptoms Scale (PANSS; [78]). In order to explore the association between certain cognitive functions in subjects with 22q11.2DS and their ability to perceive emotional expressions in faces, correlations were calculated between the behavioural indices from the experiment (see below) and the neuropsychological tests performed in the context of the main clinical assessment. We focused on different scores reflecting memory functioning, visuospatial and visual perceptual skills, processing speed, attention and executive functioning. Subscales from the Wechsler Intelligence Scale for Children (WISC-IV; [79]) or the Wechsler Adult Intelligence Scale (WAIS-IV; [80]) were used: digit span, block design, digit-symbol coding and matrix reasoning. Scores for spatial memory (Wechsler Memory Scale-III; [81]), the Rey–Osterrieth Complex Figure [82], the Benton Lines Test [83], and the concentration performance from the d2 test of attention (d2-KL; [84]) were also measured. The "similarities" subscale from the Wechsler intelligence scales was used to assess verbal skills, however only twelve participants with 22q11.2DS performed this test during their clinical assessments.

Face stimuli

Photos of Caucasian faces were adapted from previous studies where they were pretested among eleven participants and chosen because at least ten subjects agreed on the emotion expressed [85, 86]. The material consisted of 24 colour pictures of 4 people (2 females), each picture corresponding to one emotional expression (anger, disgust, happiness, fear and sadness) and neutrality. Surprise was not used due to its ambiguity in terms of valence [e.g. 87, 88]. A circular window surrounding the face was applied to discard information about background and body, and each stimulus was displayed on a mid-level grey background (see Fig. 1). To create different intensities of expression, linear continua of morphs were designed by combining neutrality and the emotion for each expression and individual face (5 emotions × 4 people = 20 morphing continua) using Morpheus Photo Morpher 1.85 (Morpheus Software, USA). 10 static pictures were extracted from each continuum (every 10 % of morph level, from 10 to 100 %) thus obtaining 10 steps of increasing intensity of expression, from the lowest expressive face (10 % morph level) to the most expressive face (100 % morph level). After this procedure, we obtained 204 pictures: 51 pictures for each of the 4 individual faces (10 morph levels × 5 emotions + the neutral face). In a first step, a pilot study was conducted with 18 control participants to create a new set of stimuli for the main experiment. Because the intensity needed to perceive the expression could vary across each emotion and each face (e.g. the perception of anger for one individual face may occur at the 40 % morph level, while it may occur

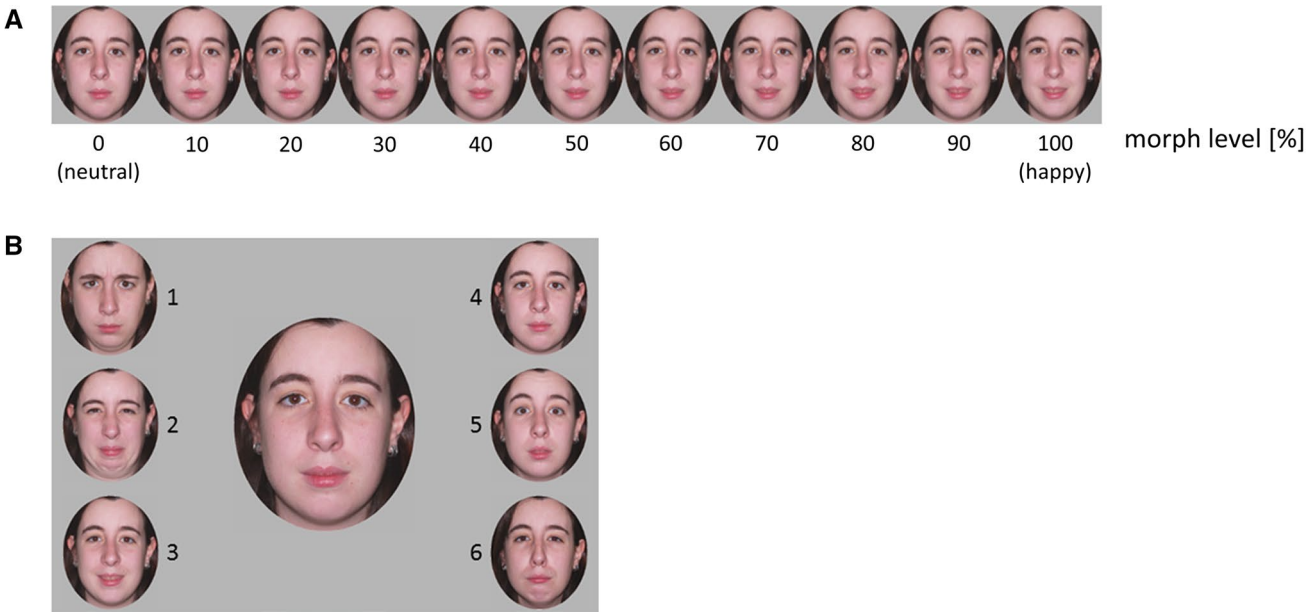


Fig. 1 **a** Example of a morphing continuum used in the main study and created by combining neutral and happy faces of the same person. Each level represents a 10 % increase in the emotion intensity (from *left* to *right*). **b** In each trial, a central face was displayed and could represent one static picture of morph between neutrality and emotion. Participants were asked to match this target stimulus with one smaller lateral face representing the six possible responses (anger, disgust, happiness, neutrality, fear and sadness)

at the 20 % morph level for another face), the goal of the pilot study was to standardise the new set of stimuli by centring all continua of morphs around the lowest intensity of expression needed to perceive the emotion. In other words, the pilot study was performed with a similar design to the present experiment (see below the "Procedure" section for all details). The lowest morph level for which the emotion was correctly perceived (i.e. the perception threshold; see below the "Analysis" section) was determined for each emotion and each individual face. In order to centre the new continua on these morph levels (i.e. to use them as the new 50 % morph levels), we considered the morph levels twice as intense as the most expressive faces (i.e. the 100 % morph levels) in the new set of stimuli. For example, if the participants in the pilot study first perceived happiness in the 30 % morph level for one face, we considered the picture corresponding to the 60 % morph level as the 100 % morph level in the new set of stimuli. Hence, after the pilot study, the morphing procedure was applied again for each emotion and each face by combining neutrality and the new most expressive faces. We thus created 20 new continua of 10 morph levels corresponding to the final set of stimuli used in the main study. Again, it was composed of 204 pictures: 51 pictures for each of the 4 individual faces (10 morph levels × 5 emotions + the neutral face). Figure 1a depicts an example of a continuum for happiness.

Procedure

Participants were tested in a silent room approximately 60 cm in front of a computer screen (15″). In each trial, seven pictures were displayed with one large (15 × 12 cm) central face and six smaller (5 × 4 cm) lateral faces (Fig. 1b). The central face was the target stimulus that had to be categorised. It could be one picture among the 204 comprising the final set of stimuli. Because the task asked for a visual matching, the lateral faces were all of the same person and corresponded to the six possible emotions that the central face could express. They represented the neutral face and the 5 most expressive faces extracted from each continua (i.e. one by emotion) composing the final set of stimuli. A digit was displayed near each one and participants were asked to determine which lateral face most matched the central one by giving the corresponding digit with an oral response. Stimuli were displayed until the participant responded. The experimenter pressed the corresponding key on the numerical pad of the keyboard to record the answer and display the next trial. After performing a training block of 4 trials to ensure that participants correctly understood the task, they performed 204 trials (corresponding to the 204 pictures of the final set of stimuli) presented in a random order within 6 blocks of 34 trials. Participants could rest between each block.

Analysis

The first analysis consisted in computing the response rates for each possible response (i.e. the perceived emotions) and for each morph level by averaging the data across the four individual faces in each participant. Figure 2 depicts these response rates within each continuum and averaged across participants in each group. To perform the statistical analyses, we then computed four indices based on the previously calculated response rates for each participant and each continuum: perception threshold, accuracy at 100 % morph level, intrusions and sharpness.

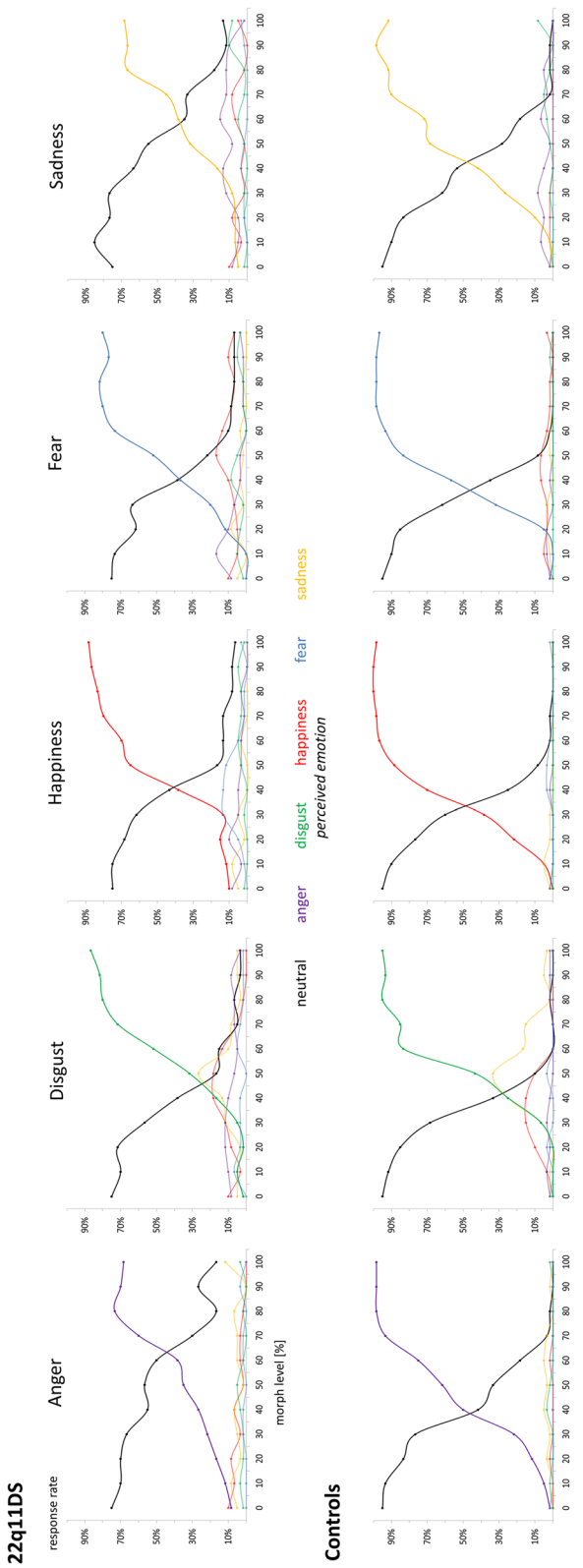
The *perception threshold* corresponded to the lowest morph level within a continuum for which the emotion was correctly perceived above chance. Because of the 6 possible responses, two successive correct responses were considered as a correct perception (less than 3 % to correctly respond by chance). For example, if the first "happiness" responses were for the 30 % and the 40 % morph levels within the happiness continuum, then the 30 % morph level was considered as the perception threshold.

Accuracy at 100 % morph level corresponded to the percentage of correct responses for the 100 % morph level within each continuum (i.e. the most expressive faces, which were the same pictures than the little lateral faces). In other words, it reflects the accuracy for the visual matching of two pictures depicting the same highly expressive faces, thus indicating a classic performance for high intensity emotional faces. For example, it was the percentage of "happiness" responses for the happy face with the highest intensity (i.e. the 100 % morph level within the happiness continuum).

Intrusions were computed according to the percentage of false perception within one continuum. In other words, intrusions indicate the percentage of times that one emotion is perceived as another one. They were computed without taking into account the "neutrality" responses that are not considered as false perception but as no perception at all. For example, the percentages of responses other than "neutral" and "happiness" (i.e. "anger", "disgust", "fear" and "sadness") within the happiness continuum were averaged together to compute the intrusion index.

Sharpness was calculated to evaluate whether emotional expressions were sharply categorised (i.e. as discrete emotion categories; see for example [89]). It reflected the abrupt change in response on either side of the threshold for each continuum to determine whether emotions were defined by clear-cut boundaries. In other words, if an emotion was sharply categorised, response rates for this emotion within its corresponding continuum would abruptly change from 0 to 100 % when emotional intensity would increase. Conversely, if this emotion was less sharply categorised, response rates would smoothly increase as emotional intensity also increases. Thus, the first step in computing the sharpness index involved calculating the global standard deviation for the neutral and the correct emotion response rates within one continuum. A sharp categorisation would be reflected in a rate of 100 % for the "neutral" responses and 0 % for the correct emotion responses in the first morph levels (i.e. for the lowest intensities), followed by an abrupt change with a rate of 100 % for the correct emotion responses and 0 % for the "neutral" responses in the last morph levels (i.e. for the highest intensities). In this theoretical case representing the greatest observable sharpening, the standard deviation computed on the 11 morph levels for both the neutral and the correct emotion response rates would be equal to 51.2 %. This value is maximal and would decrease for a less sharply defined emotional category. Hence, the second step in computing the sharpness index involved calculating the ratio between the observed standard deviation and this theoretical maximal one, with a ratio of 100 % if emotion perception is the sharpest possible. For example, if the response rates for "happiness" within the happiness continuum were 0, 0, 0, 20, 40, 60, 80, 100, 100, 100 and 100 % from the 0 % morph level (i.e. the neutral face) to the 100 % morph level (i.e. the most happy face), and those for "neutrality" within the same continuum were 100, 100, 100, 80, 60, 40, 20, 0, 0, 0 and 0 %, the standard deviation calculated from these 22 values is 43.1 %. The sharpness index is then equal to $43.1/51.2 = 84.2$ %.

To sum up, the first two indices allow characterising the performance for categorising emotions in faces depending on their intensity: the perception threshold indicates the lowest intensity needed to accurately perceive them, and accuracy at 100 % morph level provides information about the ability to recognise the most expressive faces. The last two indices further inform about the organisation of the emotional categories. Precisely, they measure how emotions are perceived and represented as discrete entities with clear-cut boundaries: intrusions indicate whether emotional categories partially overlap and may be confused, while sharpness measures whether each emotion has a clear-cut category boundary reflected by an abrupt perception as the intensity of expression increases. Although the four behavioural indices were computed from the same data, there are specificities in their calculation that leave some degrees of independence. The most expressive faces can be recognised (i.e. indicated by accuracy at 100 % morph level) regardless of the intensity needed to perceive the emotion the first time (i.e. perception thresholds), regardless of the perception of other emotions at lower intensities (i.e. intrusions) and regardless of the more or less sharp structure of the emotional category (i.e. sharpness). Intrusions and sharpness offer a measure of the organisation of the emotional categories and greater



◀ **Fig. 2** Response rates for each group of participants (*top* participants with 22q11.2DS, *bottom* control subjects) computed for each possible response (i.e. the perceived emotions) and for each morph level within each emotion continuum (from *left* to *right* neutrality-to-anger, to-disgust, to-happiness, to-fear and to-sadness). For colour information, please refer to the online version

intrusions in a morph continuum automatically reduce the corresponding sharpness. However, sharpness can be more or less abrupt without any intrusion and intrusions can be high before an abrupt perception of the emotion. Likewise, perception thresholds are automatically enhanced by greater intrusions and/or blurry emotional categories, but high perception thresholds can be observed without any intrusion and with an abrupt change of perception. Hence, the four indices evaluate different dimensions in the ability to perceive and recognise emotions in facial expressions varying in intensity, and in the underlying structure of emotional categories.

We conducted 2 × 5 ANOVAs on each index with Group (controls vs. 22q11.2DS) as a between-subject factor and Emotion (anger vs. disgust vs. happiness vs. fear vs. sadness) as a within-subject factor. Specific comparisons were made with planned comparisons. To explore whether these indices would be associated with symptomatology and/or cognitive functioning in the 22q11.2DS group, Spearman's coefficients of correlation were computed between clinical data, neuropsychological data and the four indices. These correlations were performed on a mean value averaged across all emotions for each index. Note that because the "similarities" subscale from the Wechsler intelligence scales was only performed by twelve participants with 22q11.2DS, we will not present the correlation scores calculated with this test in the main results. We will discuss this issue when addressing the limitations of the present study.

Results

Perception thresholds

There was a significant main effect of Group ($F(1, 28) = 8.19$, $p = .008$) for the perception thresholds indicating that the control group perceived emotional expressions at lower intensities (40.5 % morph level) than the 22q11.2DS group (49.6 % morph level). There was also a significant main effect of Emotion ($F(4, 112) = 17.10$,

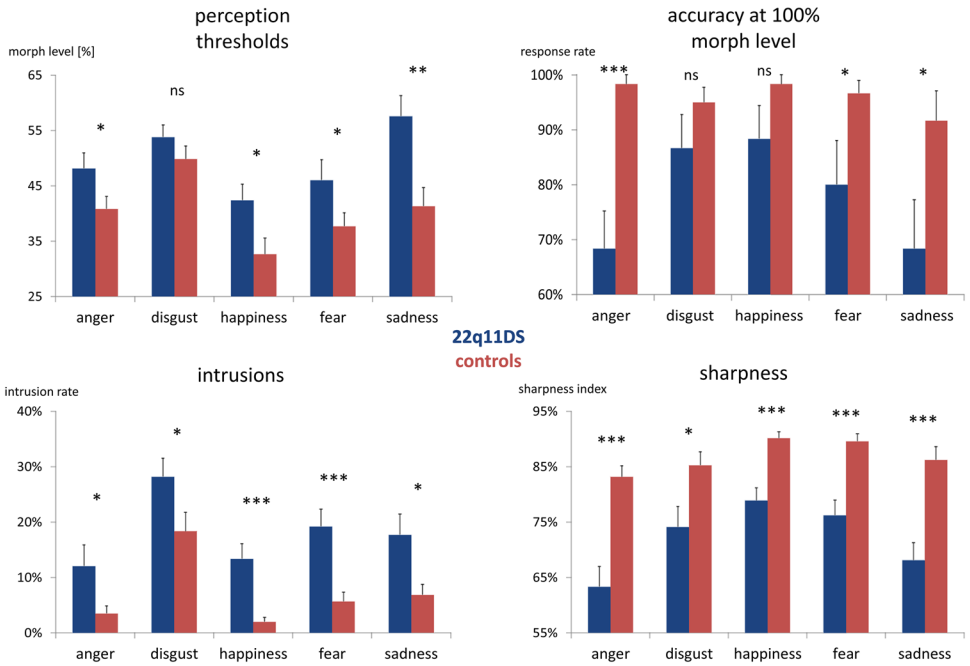


Fig. 3 Averaged perception thresholds, intrusions, accuracy at 100 % morph level and sharpness index for both groups depending on the emotion continuum (*bars* represent the standard errors; *ns* non-significant, *$p < .05$; **$p < .01$; ***$p < .001$). Note that for intrusions, group effects are depicted for each emotion continuum but no significant Group × Emotion interaction has been observed

$p < .001$) with happiness perceived at lower intensities (37.5 % morph level, all $ps < .022$), and disgust (51.8 % morph level, all $ps < .001$) and sadness (49.4 % morph level, all $ps < .018$) perceived at greater intensities than the other emotions. Interestingly, the Group × Emotion interaction was significant ($F(4, 112) = 2.63$, $p = .038$) and indicated that differences between groups were significant for anger (d = 7.3 %, $p = .049$), happiness (d = 9.8 %, $p = .022$), fear (d = 8.3 %, $p = .044$), sadness (d = 16.2 %, $p = .003$), but not for disgust (d = 3.9 %, $p = .22$). Both groups showed a significant effect of Emotion (controls: $F(4, 112) = 10.20$, $p < .001$; 22q11.2DS: $F(4, 112) = 9.54$, $p < .001$) with the same pattern of differences (i.e. happiness perceived at lower intensities; disgust and sadness perceived at greater intensities). Perception thresholds for both groups depending on the emotion are depicted in Fig. 3.

Accuracy at 100 % morph level

For accuracy at 100 % morph level (most expressive faces), there was a significant main effect of Group ($F(1, 28) = 8.46$, $p = .007$) indicating more accurate responses for the controls (96.0 %) than for the 22q11.2DS (78.3 %). The main effect of Emotion was significant ($F(4, 112) = 4.30$, $p = .003$) with lower performance for anger (83.3 %, all $ps < .046$) and sadness (80.0 %, all $ps < .032$) than for the other emotions, but the significant interaction between Group and Emotion ($F(4, 112) = 2.63$, $p = .038$) indicated that it was mainly driven by the accuracy of the 22q11.2DS group, as the effect was significant for the 22q11.2DS ($F(4, 112) = 6.74$, $p < .001$) but not for the controls ($F(4, 112) = 0.56$, $p = .69$). Moreover, differences between groups were significant for anger (d = 30.0 %, $p < .001$), fear ($d = 16.7$ %, $p = .049$) and sadness ($d = 23.3$ %, $p = .028$), but not for disgust ($d = 8.3$ %, $p = .21$) and happiness ($d = 10.0$ %, $p = .11$). Figure 3 depicts accuracy at 100 % morph level depending on the emotion for both groups.

Intrusions

Statistical analysis of intrusions indicated a significant main effect of Group ($F(1, 28) = 12.36$, $p = .002$) with the healthy control subjects suffering from less intrusions (7.3 %) than the 22q11.2DS participants (18.1 %). A significant main effect of Emotion ($F(4, 112) = 19.95$, $p < .001$) indicated a higher percentage of intrusions for disgust (23.3 %, all $ps < .001$) than for the other emotions. It also showed fewer intrusions for anger (7.8 %, all $ps < .043$) and happiness (7.7 %, all $ps < .028$) than for the other emotions. The two factors did not significantly interact for this index ($F(4, 112) = 0.42$, $p = .79$). However, intrusions for both groups depending on the emotion are depicted in Fig. 3 with each significant difference between groups indicated.

Sharpness

Analysis of the sharpness index showed a significant main effect of Group ($F(1, 28) = 24.45$, $p < .001$) with sharper emotional categories for the control group (86.9 %) than

Table 1 Spearman's correlations in the 22q11.2DS group between clinical and neuropsychological assessments (*rows*) and behavioural indices computed in the facial emotion task (*columns*)

	Perception thresholds	Intrusions	Accuracy at 100 % morph level	Sharpness
PANSS +	−.11	.12	.05	.21
PANSS −	−.06	.02	.01	.15
Spatial memory	−.18	**−.48**$^{.07}$	**.59***	**.42**$^{.11}$
Digit span	−.17	**−.60***	**.51**$^{.05}$	**.45**$^{.09}$
Block design	−.13	**−.75****	**.66****	**.76****
Rey–Osterrieth Complex Figure	−.25	**−.49**$^{.07}$	**.49**$^{.06}$	**.60***
Benton Lines Test	−.29	**−.73****	**.81*****	**.64***
Coding	−.09	−.33	.29	.09
Matrix reasoning	−.38	−.39	**.58***	.24
d2-KL	−.12	.15	−.09	−.14

Interesting coefficients (significant or with a strong trend) are in bold

PANSS + positive symptoms scale of the PANSS, *PANSS −* negative symptoms scale of the PANSS, *d2-KL* concentration performance from the d2 test of attention

* $p < .05$; ** $p < .01$; *** $p < .001$, p values are indicated for interesting trends

for the 22q11.2DS group (72.1 %). The main effect of Emotion was also significant ($F(4, 112) = 13.19$, $p < .001$) with the less sharply defined category for anger (73.2 %, all ps < .029), whereas greater sharpness indexes were observed for happiness (84.6 %, all ps < .031) and fear (82.9 %, all ps < .046) as compared to the other emotions. Group × Emotion interaction was significant ($F(4, 112) = 2.52$, $p = .045$) and indicated that differences between emotions were mainly observed in the 22q11.2DS group ($F(4, 112) = 12.83$, $p < .001$) compared to the control group ($F(4, 112) = 2.89$, $p = .025$). Differences between groups were significant for all emotions but weaker for disgust (anger: $d = 19.8$ %, $p < .001$; disgust: $d = 11.2$ %, $p = .018$; happiness: $d = 11.4$ %, $p < .001$; fear: $d = 13.4$ %, $p < .001$; sadness: $d = 18.1$ %, $p < .001$). Sharpness indices for both groups depending on the emotion are depicted in Fig. 3.

Correlations with clinical and neuropsychological data

Coefficients of correlations calculated in the 22q11.2DS group are depicted in Table 1. Correlations between symptomatology, as assessed by the PANSS, and the four indices of emotion perception performance were not significant (all ps >.45; see Table 1 for detailed ρs). Considering cognitive functioning, spatial memory ($\rho = .59$, $p = .022$) as well as matrix reasoning ($\rho = .58$, $p = .022$) was significantly correlated with accuracy at 100 % morph level. A significant negative correlation was observed between digit span and intrusions ($\rho = -.60$, $p = .019$). Block design was negatively correlated with intrusions ($\rho = -.75$, $p = .001$), and positively correlated with accuracy at 100 % morph level ($\rho = .66$, $p = .007$) and sharpness ($\rho = .76$, $p = .001$). Rey–Osterrieth Complex Figure was also correlated with sharpness ($\rho = .60$, $p = .018$). Interestingly, significant correlations were found between Benton Lines Test and intrusions ($\rho = -.73$, $p = .002$), Benton Lines Test and accuracy at 100 % morph level ($\rho = .81$, $p < .001$) and Benton Lines Test and sharpness ($\rho = .64$, $p = .010$) (Fig. 4). No other significant correlations were observed. Note that no significant correlations involving the perception thresholds were found.

Discussion

Facial emotion perception in 22q11.2DS: intensity effects and the structure of emotional categories

The present study first sought to examine whether the intensity of expression needed to perceive emotions in expressive faces is the same in children and adolescents with 22q11.2DS as in healthy age-matched control subjects. To this end, we used static pictures of morphs between neutrality and expressive faces, and we computed the perception thresholds for the different facial expressions in a visual matching task. We found higher perception thresholds in 22q11.2DS participants than in healthy controls, thus indicating that children and adolescents with 22q11.2DS need more expressive faces to accurately categorise the emotions. Because low-intensity facial expressions are frequent in everyday life, this result suggests that impaired recognition of emotional faces in people with 22q11.2DS, and more generally disturbed socio-emotional behaviour, may be partly explained by a reduced ability in categorising such ambiguous expressions.

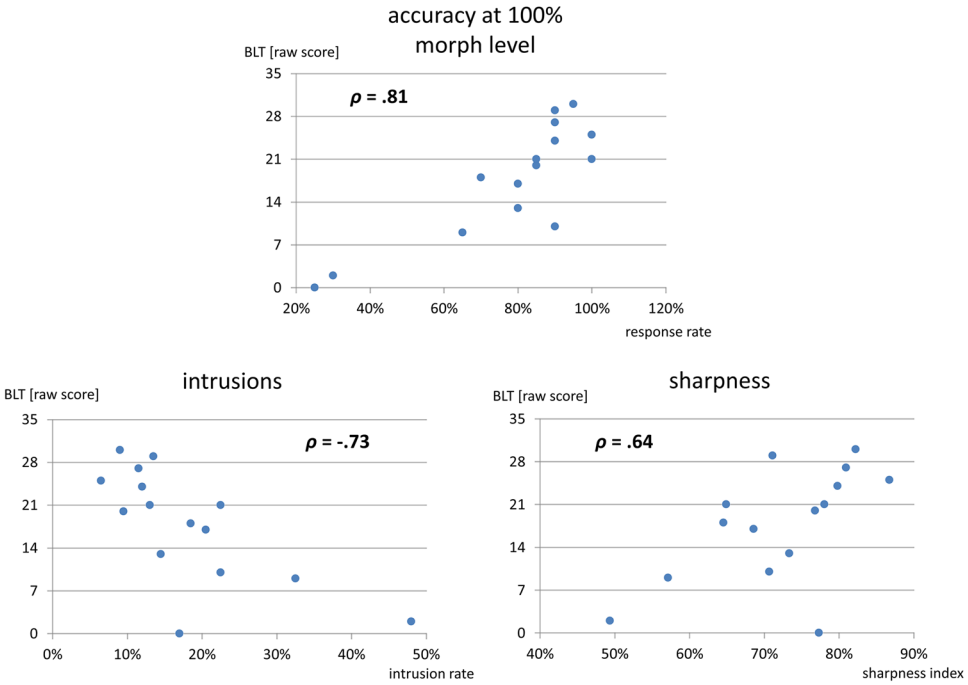


Fig. 4 Spearman's correlations in the 22q11.2DS group between the score for the Benton Lines Test (BLT) and three behavioural indices obtained in the facial emotion task (accuracy at 100 % morph level, intrusions and sharpness index)

Contrary to previous studies [62, 64, 65] which found impoverished recognition only for anger, disgust and fear in highly expressive faces, we observed lower perception performance for anger, happiness, fear and sadness, but not for disgust. Because perceiving an emotion in low-intensity expressive faces may tap different mechanisms than in highly expressive faces, we also analysed accuracy at 100 % morph level (i.e. the most expressive faces). Results indicated differences between groups of participants for anger, fear and sadness but not for happiness and disgust. Thus, the discrepancies between studies may come from methodological differences such as the task used. Indeed, in previous studies, participants were asked to identify emotions using a verbal categorisation task [62, 64, 65]. This procedure may involve verbal skills and conceptual knowledge in comparison to the visual matching task with no explicit need for labelling. Consequently, one may suggest that visual matching may have artificially enhanced the role of visual skills. However, visual abilities are important to categorise facial emotions in daily life where verbal cues are often absent in such a task. Moreover, since people with 22q11.2DS suffer more from visual than verbal impairments [52, 54, 55], and since we hypothesised that impaired visual abilities may explain their difficulties in categorising facial emotions, we specifically chose a visual matching task to mobilise visual skills and reduce the influence of verbal abilities. Note that a recent study in individuals with 22q11.2DS has indicated a distinction between the results obtained in an explicit task, and those observed with an implicit measure of the same mechanisms [90]. Hence, whereas the same underlying visual mechanisms may be at work to perceive facial emotions in different tasks, verbal labelling and visual matching of facial emotions may recruit different explicit processes that may differently influence the behavioural results. Likewise, we are not sure that an explicit visual matching task does not elicit non-visual mechanisms. As a consequence, the implicit processing of facial emotions depending on the help of visual and/or verbal cues should be investigated in future studies. Another discussion on the involvement of verbal and visual skills in emotion categorisation and the influence of the task used is presented in the "Limitations" section.

Nevertheless, the present study confirms that individuals with 22q11.2DS suffer from disturbed facial emotion recognition. They need more intense facial expressions to correctly perceive and categorise emotions. One exception was found for disgust. This null effect for disgust may be explained by the age of the participants in the present study. Indeed, according to Durand and collaborators, young healthy people have more difficulties categorising disgust, compared to other emotions, due to a slower developmental course [86]. This might explain the lack of differences between groups for this emotion. For both groups of subjects, disgust may be more difficult to perceive. However, difficulties in identifying disgust are observed until the age of 11 [86]. Twenty-four subjects among the 30 who participated in the present study were older. This clearly suggests that the age of the participants may be only one partial explanation for this result. Another conceivable explanation could be that disgust is never perceived with a low intensity in daily life. People are either disgusted or not disgusted with no intermediate levels. In support of this, we found a

high level of intrusions for disgust compared to other emotions in both groups of participants. Low-intensity disgust may frequently be perceived as another emotion (especially anger, happiness and sadness; see Fig. 1) as it does not look like a natural expression of disgust. A last explanation could be that the stimuli were not sufficiently well designed for the disgust expression. However, all stimuli were pretested and chosen because healthy participants were able to accurately categorise emotions in these pictures. Moreover, results for accuracy at 100 % morph level indicated that both groups of subjects were able to perceive disgust in the most expressive faces, even better than for other emotions in the 22q11.2DS group. Overall, the results rather suggest that disgust is a specific emotion difficult to perceive in low-intensity expressive faces and more often perceived as another emotion, at least in children and adolescents. Further investigations are needed to determine why disgust suffers from more intrusions than the other emotions even in healthy participants, and whether this specificity for disgust is also observed in adults.

By measuring intrusions and a sharpness index, the present study also aimed at providing information about the underlying organisation of emotional categories in young people with 22q11.2DS. More intrusions were observed in the 22q11.2DS group than in healthy participants, indicating less clear-cut boundaries between emotions. Likewise, facial expressions are more gradually perceived in individuals with 22q11.2DS as revealed by the sharpness index, lower in subjects with 22q11.2DS than in controls for all emotions. These results suggest that emotional categories are less sharply defined in people with 22q11.2DS. In other words, people with 22q11.2DS, in comparison to healthy participants, may perceive and represent facial emotions as less discrete entities. This leads to greater confusions between emotions and a smoother change of perception as the intensity of expression increases.

Interestingly, when considering differences between emotions, we found that perception thresholds were lower for happiness and higher for disgust and sadness compared to other emotions in both groups of participants. In addition, the sharpness index showed that happiness and fear are the sharpest emotional categories, whereas anger is the blurriest one in both groups of subjects. These patterns indicate that for both groups of subjects the differences between emotions in the intensity needed to accurately perceive them and in the shape of their representation are the same. Overall, these results suggest that the perception of emotional categories by intensity may be organised in a similar manner in 22q11.2DS and in healthy people, i.e. with the same qualitative representational architecture differentiating each basic emotion. People with 22q11.2DS may suffer more from a quantitative impairment, each category being less sharply structured and needing a higher intensity of expression to be perceived. Further studies using morphs between all facial expressions may be relevant to better delineate the structure of the emotional categories in 22q11.2DS.

Association with cognitive and emotional mechanisms

Another goal of the present study was to explore the cognitive mechanisms that may subtend the difficulties in emotional face categorisation in 22q11.2DS, and we especially suggested that the visual disabilities repeatedly observed [52, 54, 55] may explain these difficulties. Indeed, object perception [49], visuospatial skills [54–57] and visual exploration strategies [62] are disturbed in this syndrome, and deficits in visual functioning have been suggested to generally explain social difficulties in people with 22q11.2DS [52]. Results of our correlational analyses indicated that several neuropsychological tests directly assessing visual cognition or with a strong visual component (spatial memory, matrix reasoning, block design, Rey–Osterrieth Complex Figure and Benton Lines Test) were correlated with different indices of emotion perception performance, especially those related to the structure of emotional categories (i.e. intrusions, sharpness index). Hence, poor visual skills may underlie less clearly defined emotional categories in people with 22q11.2DS. Accuracy at 100 % morph level was also correlated with spatial memory, block design and Benton Lines Test, suggesting that poor visual skills also alter the visual matching of highly expressive faces.

Structural and functional abnormalities in the parietal lobe [4, 6, 16, 50, 58–61] may underlie visual impairments in people with 22q11.2DS, especially visuospatial dysfunctions associated with abnormal activities in the dorsal visual stream [e.g. 61]. It has been shown that parietal volumes are related to the ability to copy the Rey–Osterrieth Complex Figure [91], a test that was significantly correlated with different indices of emotion categorisation in the present study. Likewise, the Benton Lines Test that precisely assesses visuospatial skills was correlated with several behavioural indices (see Fig. 4). Parietal integrity is also important to perform arithmetic tasks, often inaccurate in individuals with 22q11.2DS [54, 57]. Our results indicated significant correlations between digit span and emotion recognition performance. Interestingly, as other serial short-term memory tasks, digit span has a strong visuospatial component involving parietal functions [e.g. 92]. Hence, visuospatial dysfunctions subtended by abnormalities in the visual dorsal stream may underlie certain difficulties in categorising expressive faces in individuals with 22q11.2DS. In addition, the ventral visual system may also be impaired in 22q11.2DS [50] and involved in the observed deficits in emotion perception, in association with

behavioural difficulties in perceptual tasks [49]. Thus, further studies using neuroimaging techniques may help determine whether emotion recognition is related to an impairment of the functional networks in the visual system, or whether it is only restricted to face-sensitive cerebral areas as previously suggested [70].

Non-visual cognitive disabilities may also be involved in difficulties observed in 22q11.2DS for emotional face processing. However, no correlation with neuropsychological tests assessing non-visual functions (i.e. attention, processing speed) emerged in the present study. Results are quite mixed in the literature. For example, disturbed executive functions have sometimes been related with poor social skills in 22q11.2DS [93], whereas some studies do not find the same association [30]. McCabe and collaborators have suggested that a lack of flexibility in visual scanning strategies may generally explain the difficulties observed in individuals with 22q11.2DS to process faces [62], whereas more specific dysfunctions in the face-processing network have also been found [70]. Because we did not perform a large neuropsychological assessment (see below the "Limitations" section), further studies are needed to better delineate the involvement of various cognitive functions in the categorisation of emotional faces. However, our results suggest that impaired cognitive functioning is not a critical factor in the recognition of emotional expressions by patients with 22q11.2DS.

Disturbed emotional mechanisms associated with negative symptoms may also underlie the facial expression recognition difficulties in 22q11.2DS. A recent study has indicated that memory for faces is more impaired than memory for verbal material in people with 22q11.2DS suffering from predominant negative symptoms [75]. Negative symptoms are also associated with disturbed processing of emotional faces in schizophrenia [76, 77]. Especially, the lack of emotional expressiveness in schizophrenia may underlie difficulties in emotion recognition [94, 95]. Similarly, the "emotional withdrawal and expression" component of the negative symptoms as delineated in 22q11.2DS [42, 75] has been related to socio-cognitive deficits and may be more particularly associated with the difficulties in recognising expressive faces. However, we did not find any correlation between behavioural measures of emotional face processing and the negative symptomatology of the 22q11.2DS participants. This suggests that their deficit in emotion recognition is not related to their affective functioning in the present study. Note that the global measure of negative symptoms from the PANSS may not be precise enough to tackle the "emotional withdrawal and expression" subcomponent identified by Schneider and collaborators [42, 75]. Furthermore, the task used in the present study may not have elicited emotional mechanisms as visual matching might have been performed without directly processing the emotional content of facial expressions. Future studies should be designed to precisely examine whether the affective profile of people with 22q11.2DS is involved in their disabilities for categorising emotional faces.

Limitations

The present study suffers from limitations mainly due to the correlational analyses. Indeed, non-parametric correlations performed with fifteen participants do not provide strong statistical power and the reported data must be interpreted with caution. For example, these analyses help suggest that a visual component may partly underlie the disabilities in emotion recognition observed in 22q11.2DS. We acknowledge that this result only provides preliminary evidence on the subtle mechanisms involved in facial emotion perception that could be impaired in 22q11.2DS, and that future work should further examine this issue. Moreover, in order to precisely determine whether this finding constitutes a hallmark of the syndrome, a comparison with another population presenting similar socio-cognitive impairments should be carried out.

Because our neuropsychological data were obtained in the context of the patients' main clinical assessment, another limitation is the fact that no large assessment of general cognitive functioning was carried out. In the literature, certain authors do not find any significant correlation between the recognition of facial emotional expressions and general intellectual functioning [65]. Conversely, others observe an association between IQ and visual exploration of faces [66]. Further studies are thus needed to better delineate the involvement of different cognitive functions in the categorisation of emotional faces when no verbal information is provided. In this regard, verbal skills might have been specifically investigated in the present study to show a dissociation with visual skills and reinforce our view that visual cognition is a main component of the difficulties observed in 22q11.2DS. We analysed the "similarities" subtest of the WISC/WAIS but another consequence of the restricted neuropsychological data is that it was only performed by twelve participants with 22q11.2DS. Correlations with each behavioural index did not identify any significant association (perception thresholds: $\rho = -.17$, $p = .60$; intrusions: $\rho = -.27$, $p = .41$; accuracy at 100 % morph level: $\rho = .34$, $p = .28$; sharpness: $\rho = -.02$, $p = .96$), thus supporting our interpretation. However, because of their weakness, we chose not to present these results in our main analyses.

Furthermore, as noted in the "Facial emotion perception in 22q11.2DS: intensity effects and the structure of emotional categories" section, Giersch and collaborators showed that people with 22q11.2DS are impaired in a visual discrimination of local elements embedded in global

forms when explicitly asked for. By contrast, they showed facilitated responses when exposed to implicit congruent priming of the local elements [90]. This finding suggests that people with 22q11.2DS may not be impaired in automatic and implicit visual processes, but rather in the controlled decisional mechanisms recruited during the explicit processing of visual information. In other words, the task performed may contaminate investigations of the "pure" visual mechanisms involved in facial emotion categorisation. Hence, future work is needed to determine whether early visual stages are involved in the difficulties observed in people with 22q11.2DS, and precisely disentangle the respective contribution of visual and verbal skills in categorising facial emotions. In any event, the results of the present study open up new paths for future research.

Conclusions

In conclusion, the present study shows that children and adolescents with 22q11.2DS present reduced abilities to perceive and categorise emotional expressions of faces, with expressions of greater intensity needed to perceive the emotions and with less clear-cut boundaries between emotional categories (i.e. smoother transitions between emotions). No association between facial expression recognition and negative symptoms or cognitive functions was found, except for visuospatial and visual perceptual skills which seem important to accurately perform the matching of emotional faces. If future work supports the great role of visual cognition in categorising emotions in faces for individuals with 22q11.2DS, specific rehabilitation programmes could be implemented to improve social cognitive abilities by focusing on visual skills, and/or by developing non-visual strategies to accurately categorise facial expressions. It would be also important to use expressive faces with different intensities of expression in order to help people with 22q11.2DS categorise facial emotions even when they are moderately expressed, as frequently observed in daily life.

Acknowledgments The authors wish to thank all the participants and their families who generously participated in the study. They also wish to thank the two anonymous reviewers for their constructive comments on previous versions of the paper. This research was funded by the "Conseil Scientifique de la Recherche" of Le Vinatier Psychiatric Hospital in Lyon, France.

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

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