Neurocognitive mechanisms and vulnerability to autism and ADHD symptoms in the 22q11.2 deletion syndrome

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Title: Neurocognitive mechanisms and vulnerability to autism and ADHD symptoms in the 22q11.2 deletion syndrome
Issue Date: 2015-06-10

Chapter 4

Facial emotion processing and its relation to autism and ADHD symptomatology in 22q11.2 Deletion Syndrome

Hidding, E., de Sonneville, L. M. J., van Engeland, H., Vorstman, J. A. S., & Swaab, H. Facial emotion processing and its relation to autism and ADHD symptomatology in 22q11.2 Deletion Syndrome. *Revised manuscript under review.*

Abstract

Children with 22q11.2 deletion syndrome (22q11DS) display symptoms of autism spectrum disorder (ASD) and/or attention-deficit-hyperactive disorder (ADHD). We examined whether problems in visual social information processing are related to these symptoms in 22q11DS.

Face-, facial emotion recognition and processing of abstract visuospatial information was evaluated in 45 children with 22q11DS. Relations with ASD and ADHD symptom severity were explored.

Slower, less accurate social information processing and less accurate abstract visuospatial information processing were found in children with 22q11DS. Less accurate processing of facial emotions and visuospatial information were related to more severe symptomatology.

Impairments in processing of social information may be part of a specific endophenotype of 22q11DS. Findings suggest these impairments to be possible underlying mechanisms of ASD/ADHD symptomatology.

Introduction

Children with 22q11.2 deletion syndrome (22q11DS) are at high risk to develop social problems that affect their daily functioning. Social-cognitive impairments in these children have been reported to result in social behavior problems that are part of the two major developmental disorders; autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD). Elevated rates of both disorders have been reported in 22q11DS (Schneider *et al.* 2014; Baker and Vorstman 2012; Green *et al.* 2009; Jolin *et al.* 2009; Niklasson *et al.* 2009; Vorstman et al. 2006). The quality of social cognitive abilities influences the competence in perceiving, interpreting and reacting adequately to emotions and behaviors of others (Green *et al.* 2005). Therefore, a better understanding of the relation between the quality of face and emotion recognition and the level of social impairment in individuals with 22q11DS may help to clarify the mechanisms underlying the behavioral disturbances in the social domain that are often found in 22q11DS.

The ability to correctly identify faces and their emotional states is considered to be essential in social functioning. Bruce and Young (1986) already argued that faces provide core social information for different purposes, in particular recognition of individuals and perception of emotional states (Bruce and Young 1998; Hole and Bourne 2010). However, since face and facial emotion recognition inevitably involves processing of visuospatial information, it is also important to investigate this skill of its own accord. Faces are thought to be processed on the basis of their configural organization while processing of abstract visuospatial information requires featural processing as a clear organizational structure is lacking (Hole and Bourne 2010; De Sonneville *et al.* 2002). Configural processing refers to the perception of relations among the features of a stimulus such as a face, in that the face can be seen as a meaningful whole. Featural processing is the opposite in which elements are processed piecemeal (Maurer *et al.* 2002). Recognition of facial emotions relies predominantly on configural face processing but may also be achieved through featural information processing, although this is less efficient and slower (Hole and Bourne 2010). Therefore, in order to increase insight into facial emotion processing in individuals with 22q11DS both configural and featural processing abilities need to be assessed.

Only a limited number of studies investigated face and emotion recognition in 22q11DS. Poorer accuracy of face recognition and emotion recognition has been found in comparison to healthy siblings, children with William syndrome (IQ matched) and typical controls (Campbell *et al.* 2009; Lajiness-O'Neill *et al.* 2005; Glaser *et al.* 2010; Campbell *et al.* 2010; Campbell *et al.* 2011; McCabe *et al.* 2011; Gur *et al.* 2014). In

addition, reduced tempo in remembering faces and identification of emotions has been reported in patients with 22q11DS (Gur *et al.* 2014). Accuracy of face recognition was reduced in both individuals with 22q11DS and children with idiopathic developmental delay as compared to normal control subjects (Glaser *et al.* 2010). This study also focused on the nature of face processing impairments in 22q11DS by using tasks that required featural or configural processing, respectively. Both the 22q11DS children and the children with idiopathic developmental delay displayed less accurate featural information processing compared to normal control subjects. Interestingly, the 22q11DS group also showed a decreased accuracy in configural processing, suggesting a specific impairment in visual facial processing in 22q11DS.
In studies comparing gender and age matched control subjects to individuals with 22q11DS, the 22q11DS group displayed more difficulties in identifying the facial emotions anger, disgust and fear, and also in the recognition of neutral faces (McCabe *et al.* 2011; Campbell *et al.* 2010). Jalbrzikowski *et al.* (2012) reported similar impairments, although in their study the identification of facial expressions of happiness, anger and sadness was most impaired in young adolescents with 22q11DS. Using an eyetracker, Campbell *et al.* (2010) reported atypical visual scanpath patterns in subjects with 22q11DS during facial emotion processing, compared to healthy controls. Individuals with 22q11DS spent more time on the mouth region and less on features that are important for accurate identification of emotions such as the eyes. This was also found during neutral face processing (Glaser *et al.* 2010), suggesting that individuals with 22q11DS have less adequate visual social information processing skills compared to control subjects. Only one eyetracking study compared scanpath patterns obtained during emotion recognition and during recognition of non-social stimuli (weather scene tasks) in 22q11DS (McCabe *et al.* 2011), showing that the patterns of adolescents with 22q11DS differed from those of control subjects, during processing of faces as well as processing of non-social visual stimuli. These results suggest that there may be a general visual information processing deficit besides the specific difficulties with processing of faces (McCabe *et al.* 2011).
In sum, studies thus far present evidence for less accurate visual face and emotion recognition and problems with visuospatial information in general in individuals with 22q11DS. Because of the known high risk for ASD and ADHD symptomatology in 22q11DS, it is clearly of interest to investigate whether abnormalities in visual social information processing are associated with the frequently observed symptoms in the social behavioral domain in 22q11DS. Thus far, little is known about deficits in face and facial emotion processing in subjects with 22q11DS and its relation with ASD and ADHD symptomatology. The few studies comparing face and facial emotion processing between subjects with 22q11DS and subjects with idiopathic autism, reported similar problems for both groups in memory for faces and accuracy of recognition of facial

emotions and non-social stimuli (McCabe *et al.* 2013; Lajiness-O'Neill *et al.* 2005). Patients with ASD and 22q11DS showed partly comparable patterns of scanpaths and deficits in emotion recognition, but subjects with 22q11DS took even less time looking at salient regions and spent more time looking at the mouth compared to subjects with ASD. Despite 22q11DS sharing phenotypical characteristics with ASD such as poorer facial emotion recognition, the underlying pathways of information processing might differ (McCabe *et al.* 2013). The identification of specific impairments in the processing of visuospatial information, differentiating between social and abstract visuospatial content, and elucidating their possible relation to ASD and ADHD symptomatology may help to improve our understanding of the neurodevelopmental impairments observed in 22q11DS.

The purpose of our study was to examine face and facial emotion recognition in children with 22q11DS. To find out whether impairments in these social skills are (partly) explained by impairments in the processing of visuospatial information in general, we also included a task requiring the recognition of abstract visuospatial patterns, differentiating between configural and featural processing strategies. In line with previous studies we anticipate that face and facial emotion processing in individuals with 22q11DS is impaired. Here, we hypothesized that these impairments can at least partly be explained by impairments in general visual information processing. Lastly we hypothesized less well developed visual social information processing to be related to more severe ASD and ADHD symptomatology.

Method

In the present study, 27 females and 18 males with genetically confirmed 22q11DS participated (*M*age = 13.3, SD=2.7, range 9-18.5; Full scale intelligence: *M*= 66.3, SD=12.6) . The study was part of a nationwide study. Assessment took place at the Department of Psychiatry, Brain Center Rudolph Magnus of the University Medical Centre Utrecht (UMCU) and patients were recruited via the website and newsletter of the 22q11DS parents' network in the Netherlands or via referral by various medical services. Parents and participants were informed by phone about the aims of the study and received a complete description of the study in writing before they decided on participation. Informed consent was obtained from participants and parents or caretakers. The assessment protocol was approved by the Dutch Central Committee on Research Involving Human Subjects. Assessments took place at the outpatient center of the UMCU and were carried out by an experienced child neuropsychologist and child psychiatrist.

Measures

Severity of ASD and ADHD symptomatology

Psychiatric classifications were made according to DSM-IV criteria (American Psychiatric Association 2000) resulting from a multidisciplinary consensus meeting headed by an experienced child psychiatrist, on the basis of clinically structured and semi-structured interviews (with the child and the caregivers), observation of the child, questionnaires, and assessment of intellectual functioning. The assessment protocol has been described in a previously published study (Vorstman *et al.* 2006). An overview of the DSM-IV classifications of the sample, reflecting the multidisciplinary clinical consensus based on all available patient information, is provided by Table 1.

The assessment protocol included *the Autism Diagnostic Interview-Revised* (ADI-R; Rutter *et al.* 2003), scored by certified interviewers, used to quantify autistic symptoms. The ADI-R provided scores for the three domains in which children with autism spectrum disorders (ASD) experience difficulties, i.e. reciprocal social interaction, communication impairment, repetitive and stereotyped behaviors. The classifications autism and pervasive developmental disorder not otherwise specified are both referred to as ASD.

In some cases, the DSM-IV diagnoses deviate from the classifications that would be obtained if only the outcomes of the questionnaires were used. According to DSM-IV guidelines, a diagnosis of both ADHD and ASD in one individual is not allowed (American Psychiatric Association 2000). In those cases in which the ASD symptomatology was more dominantly present explaining also the ADHD symptoms, no (additional) ADHD diagnosis was made based on such symptoms. As a consequence, only one individual was diagnosed with ADHD comorbid to an ASD diagnosis because this ASD diagnosis could not explain the severely comorbid ADHD symptomatology (Table 1).

Because of the high prevalence of both ASD and ADHD in 22q11DS the possible co-occurrence of symptoms of both disorders was also investigated. To this end, we used the three ADHD domains (inattention, hyperactivity, impulsivity), as rated with a structured questionnaire based on the criteria of DSM-IV as a measure of severity of ADHD symptoms. This questionnaire consisted of comparable items as the Conners' Rating Scales-Revised (Conners 1997) and the Dutch version of the ADHD DSM-IV rating scale (Kooij *et al.* 2008). Likewise, the three domains of the ADI-R were used as a measure of severity autism symptoms. Table 2 provides the means and distribution of the ASD and ADHD severity scores.

Table 1 ***Psychiatric classifications according to DSM-IV criteria with primary diagnoses and comorbid diagnoses.***

Diagnostic classification (primary)		*Comorbid diagnoses***				
	N	ASD	ADHD	Dep.dis	ODD*	Psych.dis
Autism spectrum disorder (ASD)	25		1	3		4
Attention Deficit Hyperactivity Disorder	0					
Anxiety Disorder	0					
Conversion Disorder	1					
Depressive disorder (Dep.dis)	2					
Psychotic disorder (Psych.dis)	1					
Without psychiatric classification	16					
Total	45		1	3		4

* Oppositional defiant disorder
** Represent comorbid diagnoses within the total N of 45

Table 2 ***Autism and ADHD severity scores.***

	N	*M*	*SD*	Range
ADHD-total	45	12.3	8.7	0-30
Inattention	45	8.4	6.4	0-23
Hyperactivity	45	1.9	2.4	0-7
Impulsivity	45	1.9	2.0	0-9
ADI-total	46	25.7	13.9	0-49
Reciprocal social interaction	46	11.5	7.1	0-26
Communication impairment	46	8.2	5.4	0-19
Repetitive and stereotyped behaviors	46	2.2	2.0	0-8

Intellectual functioning was assed using the Dutch version of the Wechsler Intelligence Scales for Children WISC-III (Wechsler 2002; Wechsler 2005b). In one case the WISC-R was used (Wechsler 1974), in four cases the adult scale (WAIS-III; Wechsler 2005a) for adolescents older than 16 years was applied. In one case information about intelligence was missing.

Visual information processing was assessed with the use of the Amsterdam Neuropsychological Tasks (ANT) program (De Sonneville, 1999; 2005). Test-retest reliability, construct-, criterion, and discriminant validity of the computerized ANT-tasks are satisfactory and have extensively been described elsewhere (De Sonneville 2014; Gunther *et al.* 2005; Rowbotham *et al.* 2009; Huijbregts *et al.* 2002). The ANT tasks, used in this study, will be briefly described, for detailed descriptions including examples of signals and timing between signals, see e.g. De Sonneville *et al.* (2002).

Face recognition (FR) With this task speed and accuracy of recognizing (neutral) faces was measured. From a set of 20 pictures of different persons (boys, girls, men and women) a probe, the to-be-recognized face, is presented on a monitor for 2.5 seconds, prior to the imperative signal which consists of four digitized high-quality color photos of human faces. Gender and age category (children, adults) of signal and probe always match. A 'yes'- response is required when the probe is present (20 trials) by pressing the mouse button below the index finger of the preferred hand, and a 'no'- response when the probe (20 trials) is not present, by pressing the mouse key below the index finger of the non-preferred hand. Main outcome variables were mean reaction time and number of errors.

Identification of Facial Emotions (IFE) This task examined the ability to identify emotions from facial expression. Participants were asked to judge whether a face showed a specific expression by pressing the 'yes'- key or another non target emotion by pressing the 'no'- key.
The total stimulus set consisted of 32 pictures from four different persons, each showing the eight emotions: happy, sad, anger, fear, disgust, surprise, shame, and contempt. The task consists of eight parts of 40 trials in which half of the trials contain the target emotion, whereas in the other half a random selection of the other emotions is presented. Four task parts were administered to measure the recognition of the basic emotions happy, sad, anger, and fear, respectively. Main outcome variables were mean reaction time and number of errors per task part.

Feature Identification (FI) This pattern recognition task assesses speed and accuracy of processing abstract visuospatial information. Subjects were asked to detect a predefined target pattern in a signal consisting of four patterns. The subject was asked to press the 'yes'-key when the pattern was present (half of the signals, 40 trials) and the 'no'-key when the pattern was not present. Two different task conditions made it possible to discriminate between featural and configural processing strategies. In the 'similar' condition, the distractor patterns looked very similar to the target pattern, inducing a featural processing strategy to detect the target. In the 'dissimilar' condition (other half of the signals) the distractors were very dissimilar to the target signal, invoking a configural processing strategy. Mean reaction time and number of errors were obtained for the similar and dissimilar conditions separately.

Statistical analyses

Main outcome parameters for analyses are z-scores, which are automatically computed by means of nonlinear regression functions that describe the relation between test age and task performance. These functions are fully implemented in the ANT program and based on norm samples varying in size between 3,100 to 6,700 subjects, depending on the task (De Sonneville, 2014), and are therefore considered to be reliable estimates of performance level. Results were examined for extreme values. As extreme values are a clinical reality in this population, z-scores ≥ 6 were set to 6 to keep these subjects in the analyses. One subject with an error rate >50% was excluded from statistical analysis as this rate is worse than chance level. In addition, missing values in the final sample are the consequence of an inability of the subject to complete difficult task parts, or skipping parts because of running out of time. As a result, degrees of freedom will slightly vary between analyses.

Comparison to the norm

To determine whether mean performance of the subjects with 22q11DS differed from the norm, i.e. differed from zero for z-scores, the intercept test of the multiple analyses of variance (MANOVA) was used. Results were evaluated per task by MANOVA, with the z-scores for speed (reaction time (RT)) and accuracy (percentage of errors) as dependent factors. In case the multivariate test was significant, the univariate results were presented as well.

Within-subject comparisons

Task conditions were used as levels of within-subject (WS) factors in repeated measures ANOVAs with speed and accuracy of performance as dependent variables respectively.

A significant WS factor effect implies that differences in performance level between the group and the norm depends on WS factor level (interaction). Faces present complex, but organized concrete visuospatial patterns. By contrasting the results of the similar and dissimilar condition of task FI it can be determined whether type of processing (featural vs. configural) differentiates children with 22q11DS from the norm. By contrasting the results of task FR and task FI it can be determined whether processing of facial information rather than processing of abstract visuospatial information (or vice versa) differentiates children with 22q11DS from the norm. Similarly, by contrasting the results of task FR and IFE, it can be determined whether

processing of facial emotions rather than processing of faces (or vice versa) differentiates children with 22q11DS from the norm.
WS factors per task were: *Signal* (similar vs. dissimilar) for task FI, and *Emotion* (positive vs. negative emotion - to reduce the number of analyses, it was decided to lump the three negative emotions together). When contrasting results across tasks, the following WS factors were used: *Pattern* (patterns vs. faces) for task FI and FR with separate contrasts for the similar and dissimilar condition of task FI, and *Facial Information* (neutral faces vs. facial emotions) for task FR and IFE.

Severity of ASD and ADHD symptomatology

Pearson correlations were calculated for the relation between severity of ASD and ADHD symptoms and visual social information processing (small effect size: r=0.1-0.23; medium: r=0.24-0.36; large: $r \geq .37$;Cohen 1992). To limit multiple testing, total symptom severity scores were used for ASD and ADHD separately.
Correlations between quality of featural information processing and symptom severity were also calculated. For the correlation analyses *Quality of featural processing* was operationalized as the difference of the similar condition score minus the dissimilar condition score. A high difference indicated poorer (slower/less accurate) featural processing. The role of Full Scale Intelligence (FSIQ) as a possible covariate was investigated.

Results

Standardized means of total group performances on all tasks of visual information processing are presented in Figure 1. Negative deviations from zero indicate more efficient performances, while positive deviations reflect worse performances.

Feature identification

Participants were less accurate, but not slower than the norm, as was shown by a significant multivariate effect for the identification of patterns [F(4,35) = 9.162, $p<.001, \eta_p^2=.511$] and univariate results revealing significant effects of accuracy in the dissimilar [F(1,38) = 7.226, $p=.011, \eta_p^2=.160$] and similar condition [F(1,38) = 20.114, $p<.001, \eta_p^2=.346$], but not for speed in both conditions ($.154<p<.469$). Children with 22q11DS compared to the norm performed worst in the similar condition, reflecting difficulties in featural processing as was indicated by a significant effect of the WS factor Signal for accuracy of processing [$F(1,39)=7.612$, $p=.009$, $\eta_p^2=.163$]. On speed no significant effect of Signal was found ($p=.279$).

Face Recognition

Subjects with 22q11DS were slower [$F(1,40) = 23.178$, $p<.0001$, $\eta_p^2=.367$] and less accurate in the recognition of faces [$F(1,40) = 83.361$, $p<.0001$, $\eta_p^2=.676$] as compared to the norm (multivariate effect [$F(2,39) = 54.631$, $p<.0001$, $\eta_p^2=.737$]).

Emotion Recognition

A significant multivariate effect of Emotion Recognition was found [$F(4,39) = 31.372$, $p<.001$, $\eta_p^2=.763$]. Participants were slower and less accurate on emotion recognition compared to the norm as was demonstrated by significant univariate results for the accuracy of processing positive emotions (happy) [$F(1,42) = 8.085$, $p=.007$, $\eta_p^2=.161$], negative emotions [$F(1,42) = 123.087$, $p<.001$, $\eta_p^2=.746$] as well as on speed of processing positive emotions[$F(1,42) = 44.951$, $p<.001$, $\eta_p^2=.517$] and negative emotions [$F(1,42) = 21.114$, $p<.001$, $\eta_p^2=.335$]. When comparing the quality of recognition of positive versus negative emotions (WS factor Emotion), no significant difference was found on speed ($p=.089$), but a significant effect was found on accuracy [$F(1,42)=56.892$, $p<.001$, $\eta_p^2=.575$], indicating that the children with 22q11DS as compared to the norm performed worst on the recognition of negative emotions.

Face recognition vs. Feature identification

The WS factor Pattern (faces vs. features) was significant on accuracy of processing [$F(2,76) = 5.456$, $p=.006$, $\eta_p^2=.126$], but not on speed ($p=.121$). WS contrast (faces vs. dissimilar patterns) revealed that accuracy of face recognition was significantly worse compared to the accuracy on dissimilar patterns [$F(1,37) = 9.423$, $p=.004$, $\eta_p^2=.203$], while no significant difference was found between accuracy of face recognition vs. similar patterns ($p=.938$).

Emotion recognition vs. Face Recognition

The WS factor Facial Information (Face vs. Emotions) was significant on accuracy of processing [F(2,76) = 28.000, *p*<.0001, η_p^2 =.424], but not on speed (*p*=.582). WS contrasts revealed that the accuracy of recognizing positive emotions was significantly better than the accuracy of face recognition [F(1,38) = 39.173, *p*<.0001, η_p^2 =.508] in the children with 22q11DS as compared to the norm. No significant difference in accuracy of processing negative emotions as compared to faces was found (*p*=.778).

Severity of ASD and ADHD symptomatology

Based on the findings, we decided to only include accuracy scores in the correlational analyses. FSIQ was related to accuracy of processing of positive and negative emotions (Table 3), children with a lower FSIQ showed more difficulties with accurate processing of emotions. No correlations were found between FSIQ and the other measures.

Regarding *Quality of featural processing* (similar minus dissimilar scores), correlations were found between accuracy of processing and severity of ADHD and ASD symptoms (Table 3). This indicates that children with less well developed featural processing skills, showed also more severe ADHD and ASD symptomatology.
Accuracy of facial emotion recognition was correlated with ASD symptomatology and accuracy of negative emotion recognition was related to ADHD symptomatology (Table 3). This indicates that children who display more difficulties with emotion processing also show more ASD and ADHD symptomatology.
Using FSIQ as a covariate, these effects remained significant for the relation between negative emotion processing and severity of symptoms (Table 3).
Using quality of featural processing as covariate removed the effect of emotion recognition and ADHD symptomatology, while the effect for ASD symptomatology remained significant (Table 3).

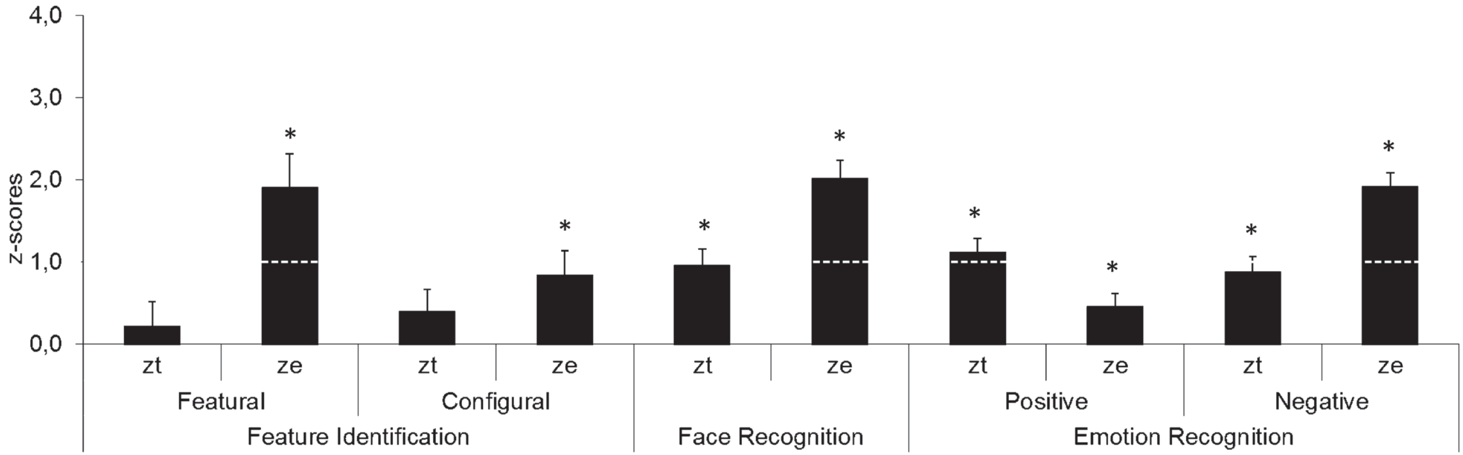

Figure 1 Mean z-scores of the total group on Feature Identification, Face Recognition and Emotion Recognition. With scores for speed (zt) and accuracy (ze) of performances. * Significant at p<0.01.

Table 3 ***Pearson and partial correlations of the accuracy scores with ASD and ADHD symptom severity***

	ASD-total	ADHD-total	FSIQ
Pearson correlations			
Quality of Featural processing	.286*	.272*	-.115
Emotion recognition (negative)	.361**	.302*	-.512**
Emotion recognition (positive)	.302*	.038	-.281*
Face Recognition	-.006	.039	-.232
Partial controlling correlations for FSIQ			
Quality of Featural processing	.270*	.273*	-
Emotion recognition (negative)	.296*	.345*	-
Emotion recognition (positive)	.256*	.037	-
Partial correlations controlling for featural processing			
Emotion recognition (negative)	.273*	.211	-
Emotion recognition (positive)	.272*	-.004	-

**Correlation is significant at the 0.01 level (1-tailed),*Correlation is significant at the 0.05 level (1-tailed)

Discussion

The purpose of our study was to investigate whether face and facial emotion recognition in children with 22q11DS is impaired and to find out whether these impairments are (partly) due to impairments in processing of visuospatial information in general. Secondly, we aimed to investigate whether identified deficits are related to severity of ASD and ADHD symptomatology.
Outcomes revealed impairments in both face and emotion recognition in subjects with 22q11DS as compared to the norm. More severe difficulties were found in recognizing negative emotions compared to positive emotions. Processing of abstract visual information was also impaired, with individuals with 22q11DS experiencing more severe impairments in featural processing of information as compared to configural processing. Processing of facial information was more severely impaired as compared to processing of abstract visual information, although no difference was found between face processing and featural processing of abstract information, suggesting that children with 22q11DS experience difficulties in the processing of complex abstract and social visual information.

Our finding of impairments in accuracy of face processing are in line with previous findings (Campbell *et al.* 2009; Lajiness-O'Neill *et al.* 2005; Glaser *et al.* 2010). We add to these results by showing that individuals with 22q11DS are also slower in processing of facial information. Because we were interested in possible face-specific deficits in visual information processing, we contrasted processing of facial information with processing of abstract visuospatial patterns, while differentiating between featural and configural processing strategies. Our results show impairments in both types of processing with featural information processing most affected, which is in line with the findings of Glaser *et al.* (2010) who found impaired featural processing of social stimuli. However, the current study gives reason to believe that this deficit in social information processing may at least partly originate from a general impairment in the processing of visuospatial information. Although processing of facial information was weaker as compared to the processing of abstract visuospatial information, comparable levels of impairments in accuracy of face recognition and processing of abstract visuospatial patterns that require featural processing were found. This could indicate that the difficulties with featural processing result in poorer processing of facial information or, alternatively, suggests that individuals with 22q11DS process faces by using a featural rather than configural strategy, which is known to be less adequate and slower (Hole and Bourne 2010).
The comparison of face recognition and the recognition of facial emotions resulted in similar levels of problems for the recognition of negative emotions but relatively less difficulties for the recognition of positive emotions. Possibly, recognition of positive emotions is relatively less influenced by a deficit in featural processing of information, as a laughing mouth stands out as a salient characteristic that can be best processed in a fast configural way. Moreover, previous studies showed that children with 22q11DS spend relatively more time looking at the mouth when processing faces (Campbell *et al.* 2010; Glaser *et al.* 2010). For positive emotion recognition the mouth area is necessary and sufficient for accurate identification while for the identification of negative emotions it is also critical to look at other features of the face, for example at the eye-brow (Beaudry *et al.* 2014; Calvo and Nummenmaa 2008).
Another aim of our study was to investigate the relation between the quality of visual social information processing and severity of ASD and ADHD symptomatology. The ability to correctly recognize faces and facial emotions is important for social behavior and deficits in this ability are possibly developmental signs of vulnerability to more social behavioral problems that are common in ASD and ADHD. We found accuracy of recognition of negative emotions to be related to severity of ASD and ADHD symptomatology. This is in line with the specific deficits in face and facial emotion processing that are found in individuals with idiopathic ASD or ADHD (Singh *et al.* 1998; Njiokiktjien *et al.* 2001; Serra *et al.* 2003; Deruelle *et al.* 2004; Yuill and Lyon

2007; Herba *et al.* 2008; Shin *et al.* 2008; Sinzig *et al.* 2008; Williams *et al.* 2008; Hole and Bourne 2010; Oerlemans *et al.* 2014). Given the deficit in processing of abstract visuospatial information which possibly underlies the deficient facial information processing, we also investigated the relation between abstract visuospatial information processing and ASD and ADHD symptomatology. Children with poorer featural processing of abstract visuospatial information showed also more ASD and ADHD symptomatology. Remarkably, when using quality of featural processing as covariate, the relation between emotion processing and severity of ADHD symptomatology no longer exists. This could indicate that in individuals with 22q11DS different mechanisms are involved in the development of social behavioral problems as compared to individuals with idiopathic ASD and ADHD symptomatology, indicating specific problems in featural processing in 22q11DS.

Although this finding needs to be replicated in a larger sample, it supports the idea of different neurobiological pathways leading to the social behavioral problems reported in developmental disorders like ASD and ADHD (Durston *et al.* 2011; De Zeeuw *et al.* 2012). Possibly, these differences in developmental pathways are the consequence of the involvement of different genetic etiology (Bruining *et al.* 2010).

The current study adds to the literature by detailed evaluation of visuospatial information processing in 22q11DS using tasks with low demands and that require less cognitive flexibility as compared to tasks in other studies. Studies comparing general visuospatial information processing and face and facial emotion processing are scarce. Therefore, the use of separate tasks for face recognition, emotion recognition, and the identification of abstract visuospatial stimuli differentiating between featural and configural processing in this study can be considered a strength. A limitation is the relatively small sample size which complicates the generalization of findings.

Conclusions

This study has shown that individuals with 22q11DS are impaired in face and facial emotion recognition as well as in processing of abstract visuospatial information. These impairments may be part of a specific endophenotype of 22q11DS. The finding that less adequate featural processing was related to more severe ASD and ADHD symptomatology, and especially that this explained the relation between quality of emotion processing and ADHD symptomatology, is important since it suggests that in 22q11DS specific mechanisms are involved in the development of ASD and ADHD symptoms as compared to idiopathic ASD and ADHD populations. However, more research into the role of visual social information processing in relation to ASD and ADHD symptomatology in larger samples is necessary.

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