Chapter 5

Social information processing in the schizophrenia spectrum: implicit attention to social signals

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Abstract

Schizophrenia is characterized by disturbances in social functioning. In the search for determinants of social dysfunction in schizophrenia patients, social cognitive capacities appear to be of crucial importance. The ability to process basic social cues, such as gaze direction and biological motion direction, quickly and automatically is thought to be a prerequisite for establishing successful social interactions and especially for construing a sense of 'social intuition'. However, studies that address the ability to automatically process such basic social cues in schizophrenia are lacking. We used a new visual illusion measuring the extent in which social cues are processed effortlessly and implicitly in three different groups characterized by the presence of traits or symptoms from the schizophrenia spectrum, i.e. 33 patients with schizophrenia, 32 siblings of patients with schizophrenia and 32 individuals with Klinefelter syndrome (47,XXY). These groups were compared to 50 age-, sex- and education-matched healthy control subjects. Results indicated that, in contrast to control subjects, patients with schizophrenia showed insensitivity to social cues. This was particularly pronounced in patients with negative symptoms. The reduced influence of social cues was also observed in first-degree relatives of patients with schizophrenia as well as in Klinefelter subjects. We suggest that the insensitivity for social cues is a cognitive aspect of schizophrenia that may be seen as an endophenotype as it appears to be present both in relatives who are at increased genetic risk and a genetic disorder associated with schizophrenia spectrum psychopathology. These social cue-processing deficits could contribute, in part, to the difficulties in higher order social cognitive tasks and hence decreased social competence that have been observed in these groups.

Introduction

One of the cardinal dysfunctions associated with the schizophrenia phenotype concerns disturbances in social functioning (DSM-IV American Psychiatric Association) (1994). Although some researchers have argued that this might be a consequence of severe psychopathology, others have demonstrated that social dysfunction is relatively independent of symptomatology (Lenzenweger et al., 1996). This view is further supported by findings that disturbances in social functioning are already present in early adolescence and often precede the onset of psychosis (Baum et al., 1995; Hans et al., 1992; Walker, 1994). In the search for determinants of social dysfunction in schizophrenia patients, cognitive capacities appear to be of crucial importance. In the last decade, there is a growing body of research demonstrating deficits in the cognitive processing of social information in schizophrenia (Pinkham et al., 2003), such as difficulties in emotion recognition (Edwards et al., 2002; Kohler et al., 2004) and the inability to understand and manipulate other people's behavior in terms of their mental states, also called Theory of Mind (Frith, 1992). Furthermore, schizophrenia patients have difficulties in the recognition of abstract social signals, such as inferences regarding actors' affect and goals (Corrigan et al., 1993). These deficits seem to be independent of intelligence, i.e. not attributable to a generalized performance deficit (Corrigan, 1994), but are related to negative symptoms such as withdrawal (Corrigan et al., 1994) and skills to receive, process, and send social signs (Corrigan et al., 1995).

An important underlying characteristic of successful social interaction is the ability to quickly process social information (Frith et al., 1999). Basic elements of a social signal that are processed fast and automatic are for example gaze direction, head orientation and body postures (Jellema et al., 2005). These cues can give clues about someone's intentions, goals and believes (Perrett, 1999). Usually, these basic social cues are largely automatically processed, which is necessary to continuously infer the meaning of the rapidly changing social signals. Moreover, it is suggested that the ability to process these basic social cues quickly and automatically is a prerequisite for establishing successful social interactions and communication (Frith et al., 1999). It may be especially relevant for construing a sense of 'social intuition', as such implicit learning processes form the basis of social intuition (Lieberman, 2000). Intuitions have been described as following: "intuitions are fast and take into account nonconsciously generated information, gathered from experience, about the probabilistic structure of the cues and variables relevant to one's judgments, decisions, and behavior" (Bruner, 1960). Although schizophrenia patients seem to fail in areas

of social intuition and automaticity in social interactions as observed in their social behavior (Bellack et al., 1990), studies that address the ability to automatically process such basic social cues in schizophrenia are lacking.

Therefore, we used a new paradigm involving a bias in the judgment of the distance between two agents induced by the automatic processing of social cues conveyed by these agents (Jellema et al., 2004). The social cues consisted of the direction of attention and implied goal-directed actions. Typically, these social cues induce the sensation of people (dis-)engaging in social interaction when their gaze or body postures are attended towards (or away from) each other. Therefore, the social cues of gaze direction and implied biological motion used in the present paradigm results in people judging the persons as closer together compared to reference objects whilst this is not the case objectively.

In addition to patients with schizophrenia and healthy controls, we also included 2 other groups in the study: a) individuals at increased genetic risk for schizophrenia, i.e. sibling of schizophrenia patients and b) individuals with an X chromosomal disorder and high levels of schizotypal traits, i.e. men with Klinefelter syndrome. Biological siblings of patients have been shown to be at significantly higher risk for the development of schizophrenia (Gottesman, 1991) and display cognitive deficits that are also seen in schizophrenia patients, although to a lesser degree (Sitskoorn et al., 2003). Inclusion of the sibling group enables the study of social cognitive deficits related to a genetic vulnerability to schizophrenia without confounding environmental influences as hospitalization, medication and psychopathology. Support favoring the role of genetic mechanisms in social cognitive deficits is derived from studies demonstrating abnormalities in the processing of social-emotional cues in biological relatives of patients with schizophrenia (Loughland et al., 2004; Toomey et al., 1999). This fits with the finding that social skills are under considerable genetic control in the general population. Men with Klinefelter syndrome have an extra X chromosome (47,XXY chromosomal pattern), and display abnormal brain development (Shen et al., 2004), social cognitive impairments (van Rijn et al., 2006b) and psychopathology that is also seen in patients with schizophrenia (Van Rijn et al., 2006a). An additional advantage arising from studying Klinefelter men is knowledge of the precise genetic etiology of this syndrome, in contrast to what is known of the genetic underpinnings of social cognitive impairments in schizophrenia. Including XXY men might point to a role of the X chromosome in development of cognitive systems that are important for processing basic social signals (cf. Skuse, 2005). Involvement of sex chromosomes might explain, in part, the sex

differences that have been observed in social cognitive skills in the general population as well as in schizophrenia populations (Hampson et al., 2006; McClure, 2000; Scholten et al., 2005).

The aim of the present study was to investigate sensitivity to basic social cues in individuals with schizophrenia, individuals with an increased genetic risk for schizophrenia and individuals with a genetic disorder and high levels of schizotypal traits. To this end we used a social distance judgment task that included two social cues, social attention (gaze direction) and implied biological motion (Jellema et al., 2004). It was hypothesized that patients with schizophrenia would demonstrate difficulties in the automatic processing of social cues compared to control participants, i.e. patients may show no response bias congruent with the direction of the social cues. Furthermore, the relationship between symptomatology and social cue processing is investigated. We predicted that the problems in social cue processing would be especially prevalent in patients with negative symptoms, since patients with negative symptoms are characterized by social-emotional disturbances. We hypothesized that siblings of patients with schizophrenia as well as XXY men would show a deviant pattern comparable to patients, although to a lesser extent. This would indicate that deficient processing of basic social cues forms part of the genetic vulnerability for the disease, possibly involving genes on the X chromosome, rather than environmental factors such as medication and potential toxic effects of psychosis.

Methods

Participants

33 Patients (23 men, 10 women) with a diagnosis of schizophrenia were recruited at the University Medical Center Utrecht. All patients met the DSM-IV criteria for schizophrenia, as confirmed by the Comprehensive Assessment of Symptoms and History interview (CASH) (Andreasen et al., 1992) administered by a psychiatrist. Patients were also screened for affective disorders, i.e. depression and mania, substance-related disorders by the CASH. Most patients were diagnoses with paranoid schizophrenia (n=22), one with disorganized type, one with residual type, six with undifferentiated type and three with schizophreniform disorder. Most patients were clinically stable and in residual state and four patients were inpatients and 29 were outpatients. Patients were all clinically stable, 31 patients received medication (30 patients only antipsychotics, such as leponex (n=13), quetiapine (n=4), olanzapine (n=6),

risperidone (n=8) and one patient also received oxazepam). Symptoms and severity were independently rated by two raters with the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). Raters were trained by a qualified trainer and followed interrater reliability training every six months. Mean positive symptoms was 14.22 (SD 5.22, range 7-27), negative symptoms 14.84 (SD 5.78, range 7-29) and general psychopathology 26.66 (SD 6.84, range 17-47). Most patients were in remission, residual state and were outpatients (29 outpatients and 4 inpatients). Mean duration of illness was 9.44 years (SD 8.01) and mean age of onset was 23.83 years (SD 5.45).

32 Siblings of patients with schizophrenia (12 men, 20 women) were recruited through advertisements at the Ypsilon website, which is a website dedicated to relatives of patients with schizophrenia. The diagnosis of schizophrenia for the affected sibling was confirmed with a CASH interview (Andreasen et al., 1992). However, due to ethical reasons we were unable to verify the diagnosis of schizophrenia for 12 affected siblings with the CASH interview.

32 Men with Klinefelter syndrome (47,XXY) were studied. The participants were recruited from the Dutch Klinefelter Association, and were not selected for psychological, behavioral or cognitive abnormalities. Diagnosis of Klinefelter syndrome was confirmed by karyotyping, using standard procedures. 50 Non-psychiatric control participants (31 men, 19 women) were drawn from the general population via advertisements in local newspapers.

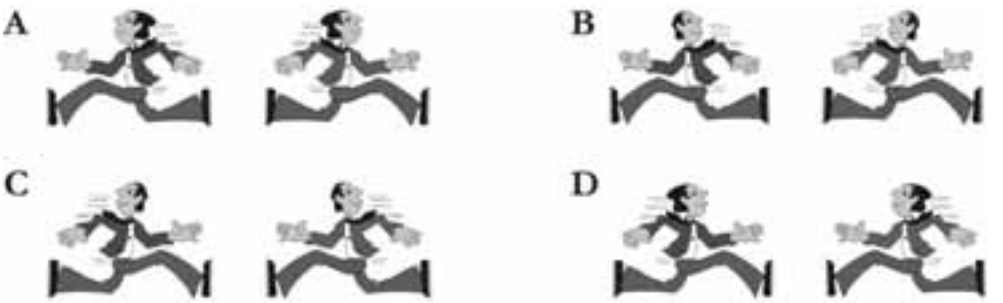
Inclusion criteria for all participants were age between 18 and 65 years and good physical health. Exclusion criteria were neurological conditions, history of head injury with loss of consciousness, recent history of alcohol and substance abuse, or mental retardation. None of the control participants and siblings had a history of psychiatric illness or use of psychiatric medication confirmed with the Mini International Neuropsychiatric Interview plus (MINI) (Sheehan et al., 1998). The local ethics committee approved the study and all subjects provided written informed consent after the procedure had been fully explained, according to Declaration of Helsinki. The Dutch translation of the National Adult Reading Test (NART) (Schmand et al., 1991) and Raven's Advanced Progressive Matrices (Raven et al., 1993) were used to match the groups on estimates of verbal and performance intelligence level, respectively (Lezak, 1995).

Social Distance Judgment Task

The Social Distance Judgment Task measures the illusion of de- or increasing distance caused by the automatic processing of social cues (Jellema et al., 2004). It is hypothesized that the perceived distance between the agents will be influenced by the social cues conveyed by the agents, resulting in a response bias paralleling the strength of social cues, which has been confirmed by pilot data from our lab. Stimuli were pairs of two cartoon figures shown in running postures conveying two different social cues: gaze direction (figures looking away or towards each other) and implied biological motion (figures running away or towards each other). Head and body of the cartoon figures were pointing in the same direction, or in opposite directions, amounting to a total of four different compositions of cartoon figures, see figure 1.

Figure 1

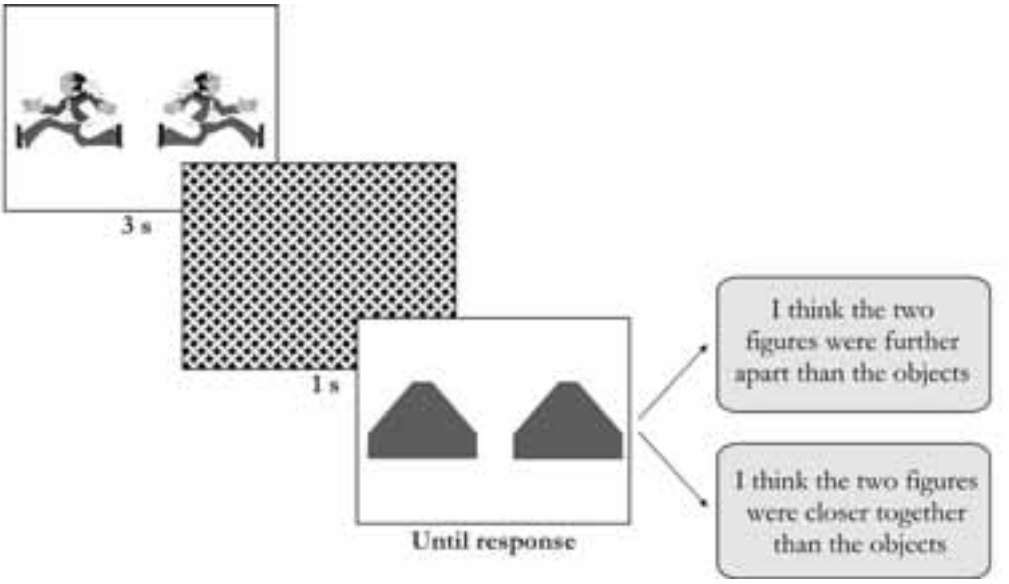
From left to right: increasing strength of social cues leading to underestimation of the distance between the cartoon figures, i.e. the response: 'I think the two cartoon figures were closer together than the two geometrical objects'.



A pair of cartoon figures was presented for 3 s, after which a mask of 1 s was shown, followed by a pair of geometrical figures (see figure 2 for an example of a trial). Participants had to choose one of two possible responses: (1) 'I think the two cartoon figures were closer together than the two geometrical objects', and (2) 'I think the two cartoon figures were further away from each other than the two geometrical objects'.

Except for the catch trials, the distance between the geometrical figures was always the same as the distance between the cartoon figures and three different distances were randomly presented: 2, 3 and 4 cm. In the catch trials the distance between the geometrical figures was different (2 cm) from the distance between the cartoon figures. The catch-trials were used to allow exclusion of those participants from analysis who did not pay proper attention to the task. Participants who made more than two errors in the catch-trials were excluded from the analyses.

Figure 2
Example of a single trial.



Results

As only males are affected with Klinefelter syndrome, two separate analyses were performed. One for schizophrenia patients and relatives, including both males and females, and one for Klinefelter men, including XXY men and male controls. 5 Patients with schizophrenia, 3 siblings, 3 Klinefelter men and 4 control participants made more than two errors in the catch-trials and were not included in further analysis.

Schizophrenia patients and relatives

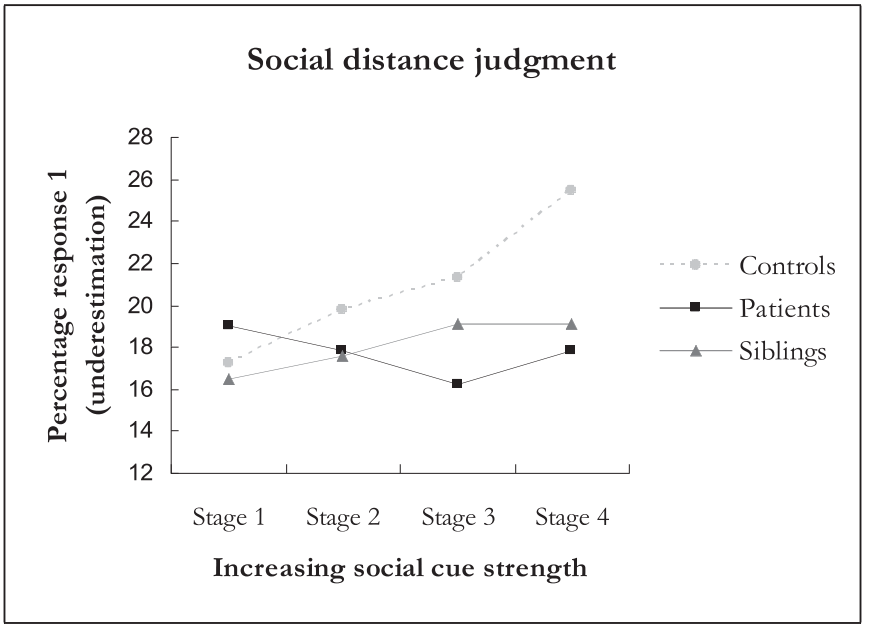
28 Patients with schizophrenia, 29 siblings of patients with schizophrenia and 46 control participants were included in the analyses, see table 1 for demographic data. A GLM repeated measures test of within subject contrasts with increasing social cue strength as within subjects variable (with 4 strength levels) revealed a significant linear increase in percentage of response 1 ("I think the two figures are closer together than the two geometrical figures") in the control group, $F(1,45)=14.27$, $p=0.0005$. In contrast, percentage response 1 did not change with increasing social cue strength of in the patient group, $F(1,27)=0.34$, $p=0.56$. Remarkably, absence of a response bias was also found in the sibling group , $F(1,28)=0.77$, $p=0.39$. The sensitivity for social cues differed significantly between patients with schizophrenia, siblings and control subjects, revealed by different patterns of percentage response 1 with increasing strength of social cues, $F(2,100)= 3.79$, $p=0.026$ (figure 3). Post-hoc tests revealed the control group to differ significantly from the patient group in sensitivity for social cues ($F(1,72)=8.06$, $p=0.006$). The sibling group did not differ from the control group ($F(1,73)=2.21$, $p=0.14$), nor from the patient group ($F(1,55)=1.09$, $p=0.30$).

Table 1
Demographic data of 28 patients with schizophrenia, 29 siblings of patients with schizophrenia and 46 healthy control participants included in the Social Distance Judgment Task.

Variable	Patients	Siblings	Control subjects	P
Age in years (SD)	32.43 (7.51)	34.62 (10.72)	31.89 (9.19)	0.45
Male:female ratio	18:10	11:18	27:20	0.11
Education in years (SD)	14.29 (2.80)	16.21 (1.93)	14.89 (2.58)	0.01*
Parental education in years (SD)	13.97 (2.98)	14.67 (2.68)	13.20 (2.89)	0.27
NART (SD)	103.56 (8.16)	104.54 (8.11)	107.63 (9.54)	0.13
Raven's (SD)	NA	109.21 (9.93)	108.40 (13.75)	0.79

- P<0.05, Between-groups comparisons with Student's t-tests, except Male:female ratio is analyzed with non-parametric Kruskal Wallis test, df =100; NA= Not available

Figure 3
Increasing social cue strength resulted in a linear increase in response 1 ('I think the two cartoon figures were closer together than the two geometrical objects') in healthy control subjects, but not in patients or sibling of patients.



Social distance judgment and symptomatology in schizophrenia patients

There was a significant negative correlation between the response bias due to social cue strength and negative symptoms of schizophrenia as measured with the Positive and Negative Syndrome Scale (PANSS), r=-0.39, p=0.04. This suggests that patients with more negative symptoms are less influenced by social cues. There were no correlations between positive symptoms or general psychopathology as measured with the PANSS and influence of social cues.

Klinefelter men

A group of 29 Klinefelter men was compared to 25 control men, see table 2 for demographic variables. A GLM repeated measures test of within subject contrasts revealed that in the control group, the social cues did elicit a response bias congruent with the directions of the social cues. We observed a significant linear increase in underestimations (i.e. increase in percentage response 1) of the perceived distance as strength of the social cues would increase, $F(1,24)=13.54$, $p=0.001$. Sensitivity for social cues differed significantly between the Klinefelter men and controls, as reflected by different patterns of percentage response 1 over the four conditions (group effect in GLM repeated measures of within subject contrasts; $F(1,52)=4.4$, $p=0.04$). Although strength of the social cues increased, percentage response 1 remained at the same level in the Klinefelter group, $F(1,28)=0.001$, $p=0.98$. The absence of a response bias congruent with direction of the social cues indicated that the distance judgment performance in this group was not influenced by social interpretation and thus more accurate compared to controls. Results are presented in figure 4.

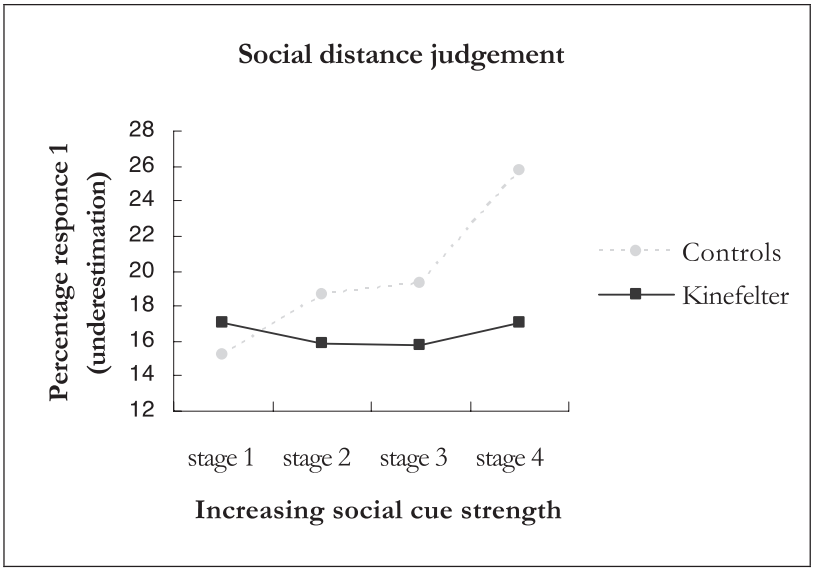
Table 2

Demographic data of 29 Klinefelter men and 25 control men.

Variable	Klinefelter men	Control men	P
Age (in years)	38.07 (8.47)	33.84 (8.90)	0.08
Education (in years)	13.92 (2.65)	14.36 (2.66)	0.56
NART (SD)	102.67 (8.61)	107.20 (10.03)	0.09
Raven's (SD)	107.68 (14.37)	111.71 (9.20)	0.24

P: Between-groups comparisons with Student's t-tests, df =52

Figure 4
Increasing social cue strength resulted in a linear increase in response 1 ('I think the two cartoon figures were closer together than the two geometrical objects') in healthy control subjects, but not in Klinefelter men.



Discussion

This study examined automatic processing of basic social cues, i.e. implied biological motion and gaze direction in three different groups: a) schizophrenia patients, b) individuals at increased genetic risk for schizophrenia, i.e. sibling of schizophrenia patients and c) individuals with an X chromosomal disorder and high levels of schizotypal traits, i.e. men with Klinefelter syndrome.

In healthy controls, an increasing strength of social cues in the stimuli was accompanied by an increasing illusion of the perceived distance between the stimuli, indicating that social cues affected decision making as we expected. In contrast, in schizophrenia patients, siblings of patients and Klinefelter men, an increasing strength of social cues in the stimuli did not have any effect on the perceived distance between the stimuli, indicating that social cues were not incorporated in the process of judging the stimuli. When considering the groups separately, schizophrenia patients and Klinefelter men showed to be less sensitive to social cues compared to controls. Performance of the siblings of patients was in between patients and control participants, that is siblings did not

differ significantly from either controls or patients. The differences can not be ascribed to differences in general cognitive function, as the groups were matched on education and intelligence estimates. Furthermore, the subjects included in the analysis understood the task and were able to perform the task correctly, as is evidenced from their lack of errors on the catch trials.

These results suggest that patients with schizophrenia demonstrated a lack of sensitivity to even basic, simple social cues, instead of deficits only in more abstract, higher-order social cue recognition (Corrigan et al., 1993). A failure to automatically and quickly process these basic social cues may contribute to difficulties in social intuition and hence coping with social situations in these patients. Also, because less basic social information is available, more widespread effects on ('upstream'-) higher-order social cognitive processing can be expected. The observed insensitivity to social cues may underly social cognitive deficits and social dysfunction in schizophrenia. The ability to process social cues automatically is thought to be especially important for theory of mind, i.e. deducing someone else's intentions, goals and believes (Perrett, 1999) and deficits in the automatic processing of these social cues might lead to disturbances in the attribution of mental states to others (Frith et al., 1999). Indeed, a recently published study demonstrates that patients with schizophrenia were impaired in using appropriate language to describe Theory of Mind animations (Russell et al., 2006).

Our results showed that especially patients with negative symptoms, which comprise social and emotional withdrawal, were insensitive to the influence of the social cues in their judgments. Patients with negative symptoms typically show problematic social functioning (Dickerson et al., 1996, 1999; Van Der Does et al., 1996), but also deficits in other social emotional tasks (Kohler et al., 2000; Mandal et al., 1998; Martin et al., 2005; Schneider et al., 1995). Thus, these results corroborate previous research demonstrating that patients with schizophrenia show deficits in the processing of social information (Pinkham et al., 2003), with more severe impairments in patients with negative symptoms (Corcoran et al., 1995; Kohler et al., 2000; Leitman et al., 2005; Mandal et al., 1999). However, this study extends previous research in demonstrating deficits in the effortless processing of simple social cues.

Interestingly, the absence of influence of the social cues on distance judgments was also observed in individuals at increased genetic risk for schizophrenia (relatives of patients) and individuals with a genetic disorder associated with increased schizophrenia spectrum pathology (Klinefelter syndrome). Based on these findings three important conclusions can be drawn.

First, siblings as well as the Klinefelter men were not clinically psychotic and did not use antipsychotic medication. The lack of sensitivity for social cues could thus not be due to the effects of illness or the medication use. In that way, these results validate the observed results in patients. Second, we propose that the observed lack of sensitivity for social cues is related to a genetic vulnerability to schizophrenia. The results showed that there were no differences between patients and siblings in distance judgment, suggesting that siblings resemble patients in an absence of automatic processing of social cues. However, one could also argue that siblings perform normally, as they also did not differ from controls. When taking the within group analysis into account we demonstrated that siblings, in contrast to normal controls, did not show a linear increase in underestimations, i.e. their distance judgments were not influenced by the social cues of human figures running towards each other or looking towards each other. Thus, our findings imply that performance of siblings resembles the lack of sensitivity to social cues observed in schizophrenia patients, albeit to a lesser extent. Moreover, our results mirror and extend previous studies demonstrating impairments in other types of social emotional cue processing in relatives of patients with schizophrenia such as recognizing emotional facial expressions (Loughland et al., 2004; Toomey et al., 1999), suggesting that insensitivity for social cues might be regarded as a genetic vulnerability to schizophrenia. Third, additional evidence for a genetic loading on social cue processing comes from the findings in individuals with a genetic disorder. Performance in the social cue task was indistinguishable between schizophrenia patients and Klinefelter men. As this disorder is defined by an X chromosomal abnormality, impaired cognitive processing of social cues in this group can be regarded as the expression of X-linked genetic pathology. Klinefelter men also display impairments in higher order social cognitive processing, such as recognition of facial expressions (van Rijn et al., 2006b). As insensitivity to social cues seems an endophenotype that is shared by schizophrenia patients and Klinefelter men, this deficit may have a common genetic (X-linked) origin in both syndromes.

Notably, individuals with autism, a disorder of the 'social brain' as indicated by deficits in theory of mind, facial affect recognition and reciprocal social behavior, also demonstrate an insensitivity to social cues using this task (Jellema et al., 2004). Hence, this study gives converging evidence that attention to basic, typically effortlessly processed social cues may belong to the fundamental cognitive operations needed for successful social behavior. With regard to the neural correlates involved in the processing of biological motion and social attention, the superior temporal gyrus, medial prefrontal cortex and anterior

cingulate have been implied (Jellema et al., 2005). Both in schizophrenia patients as well as relatives, abnormalities in these regions have been reported (Ashton et al., 2000; Dolan et al., 1995; Fletcher et al., 1999; Mitelman et al., 2005; Rajarethinam et al., 2000; Shenton et al., 2001; Takahashi et al., 2004). Interestingly, structural abnormalities in the anterior cingulate and the superior temporal gyrus have been found in Klinefelter syndrome as well (Shen et al., 2004). Additional evidence for a role of the X chromosome in development of the superior temporal gyrus comes from studies with individuals with X monosomy, showing that volume of this region is dependent on parental origin of the X chromosome (Kesler et al., 2003). It is suggested that these neural correlates also underlie Theory of Mind capabilities (Frith et al., 1999; Siegal et al., 2002).

Future studies should relate neural substrates of social cue processing in schizophrenia and relatives together with measures of social functioning. This would elucidate the relationship between the ability to process social cues and social behavior and its underlying brain pathology in schizophrenia and provide more insight into the biological vulnerability to schizophrenia. Such research should also take into account the role of the amygdala, which has been implied in social information processing (Adolphs et al., 1998). Abnormalities of the amygdala have been documented in patients with schizophrenia (Aleman et al., 2005) as well as their relatives and Klinefelter patients (Van Rijn et al., 2005).

In summary, this study allowed the investigation of sensitivity to simple, basic social cues that are usually effortlessly processed, i.e. implied biological motion and gaze direction, in individuals with a) a diagnosis of schizophrenia b) an increased risk for schizophrenia (relatives of patients) and c) with a genetic disorder associated with increased schizophrenia spectrum pathology (Klinefelter syndrome). Results showed that patients with schizophrenia, siblings of patients with schizophrenia and Klinefelter men (47, XXY) did not process these social cues automatically compared to healthy controls. Within the schizophrenia group, this was especially the case in patients with more severe negative symptoms, i.e. patients that show additional social emotional disturbances. Hence, social cue processing deficits seem related to the vulnerability to schizophrenia, instead of illness in general and with a potential involvement of genes on the X chromosome. These basic social cue processing deficits might underlie impairments in other aspects of social cognition and social functioning. Future research should investigate further the relationship between insensitivity to social cues, social functioning and neurobiological substrates in schizophrenia.

References

A.P.A. (1994). Diagnostic and statistical manual of mental disorders (4th ed.). Washington, DC: American Psychiatric Association Press.

Adolphs, R., Tranel, D., & Damasio, A. R. (1998). The human amygdala in social judgment. Nature, 393(6684), 470-474.

Aleman, A., & Kahn, R. S. (2005). Strange feelings: Do amygdala abnormalities dysregulate the emotional brain in schizophrenia? Progress in Neurobiology, 77(5), 283-298.

Andreasen, N. C., Flaum, M., & Arndt, S. (1992). The comprehensive assessment of symptoms and history (cash): An instrument for assessing diagnosis and psychopathology. Archives of General Psychiatry, 49(8), 615.

Ashton, L., Barnes, A., Livingston, M., & Wyper, D. (2000). Cingulate abnormalities associated with panss negative scores in first episode schizophrenia. Behavioural Neurology, 12(1-2), 93.

Baum, K. M., & Walker, E. F. (1995). Childhood behavioral precursors of adult symptom dimensions in schizophrenia. Schizophrenia Research, 16(2), 111.

Bellack, A. S., Morrison, R. L., Wixted, J. T., & Mueser, K. T. (1990). An analysis of social competence in schizophrenia. The British Journal Of Psychiatry: The Journal Of Mental Science, 156, 809-818.

Bruner, J. (1960). The process of education. Cambridge, MA: Harvard University Press.

Corcoran, R., Mercer, G., & Frith, C. D. (1995). Schizophrenia, symptomatology and social inference: Investigating "theory of mind" in people with schizophrenia. Schizophrenia Research, 17(1), 5-13.

Corrigan, P. W. (1994). Social cue perception and intelligence in schizophrenia. Schizophrenia Research, 13(1), 73.

Corrigan, P. W., & Green, M. F. (1993). Schizophrenic patients' sensitivity to social cues: The role of abstraction. American Journal of Psychiatry, 150(4), 589.

Corrigan, P. W., Green, M. F., & Toomey, R. (1994). Cognitive correlates to social cue perception in schizophrenia. Psychiatry Research, 53(2), 141.

Corrigan, P. W., & Toomey, R. (1995). Interpersonal problem solving and information processing in schizophrenia. Schizophrenia Bulletin, 21(3), 395-403.

Dickerson, F., Boronow, J. J., Ringel, N., & Parente, F. (1996). Neurocognitive deficits and social functioning in outpatients with schizophrenia. Schizophrenia Research, 21(2), 75.

Dickerson, F., Boronow, J. J., Ringel, N., & Parente, F. (1999). Social functioning and neurocognitive deficits in outpatients with schizophrenia: A 2-year follow-up. Schizophrenia Research, 37(1), 13.

Dolan, R. J., Fletcher, P., Frith, D., Friston, K. J., Frackowiak, R. S. J., & Grasby, P. W. (1995). Dopaminergic modulation of impaired cognitive activation in the anterior cingulate cortex in schizophrenia. Nature, 378(6553), 180.

Edwards, J., Jackson, H. J., & Pattison, P. E. (2002). Emotion recognition via facial expression and affective prosody in schizophrenia: A methodological review. Clinical Psychology Review, 22(6), 789-832.

Fletcher, P., McKenna, P. J., Friston, K. J., Frith, C. D., & Dolan, R. J. (1999). Abnormal cingulate modulation of fronto-temporal connectivity in schizophrenia. Neuroimage, 9(3), 337.

Frith, C. D. (1992). The cognitive neuropsychology of schizophrenia. Hillsdale, NJ: Laurence Erlbaum Associates.

Frith, C. D., & Frith, U. (1999). Interacting minds--a biological basis. Science, 286(5445), 1692-1695.

Gottesman, I. I. (1991). Schizophrenia genesis: The origin of madness. New York: Freeman.

Hampson, E., van Anders, S. M., & Mullin, L. I. (2006). A female advantage in the recognition of emotional facial expressions: Test of an evolutionary hypothesis. Evolution and Human Behavior, 27(6), 401.

Hans, S. L., Marcus, J., Henson, L., Auerbach, J. G., & Mirsky, A. F. (1992). Interpersonal behavior of children at risk for schizophrenia. Psychiatry, 55(4), 314-335.

Jellema, T., Lorteije, J. A. M., van Rijn, S., van t'Wout, M., de Heer, F., & de Haan, E. H. F. (2004). Failure to automate the semantic processing of social cues in autism. Perception, 33, 101-101.

Jellema, T., & Perret, D. I. (2005). Neural basis for the perception of goal-directed actions. In A. Easton & N. J. Emery (Eds.), The cognitive neuroscience of social behavior. New York: Psychology Press.

Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The positive and negative syndrome rating scale (panss) for schizophrenia. Schizophrenia Bulletin, 13, 261-276.

Kesler, S. R., Blasey, C. M., Brown, W. E., Yankowitz, J., Zeng, S. M., Bender, B. G., et al. (2003). Effects of x-monosomy and x-linked imprinting on superior temporal gyrus morphology in turner syndrome. Biological Psychiatry, 54(6), 636-646.

Kohler, C. G., Bilker, W., Hagendoorn, M., Gur, R. E., & Gur, R. C. (2000). Emotion recognition deficit in schizophrenia: Association with symptomatology and cognition. Biological Psychiatry, 48(2), 127-136.

Kohler, C. G., & Brennan, A. R. (2004). Recognition of facial emotions in schizophrenia. Current Opinion in Psychiatry, 17(2), 81.

Leitman, D. I., Foxe, J. J., Butler, P. D., Saperstein, A., Revheim, N., & Javitt, D.C. (2005). Sensory contributions to impaired prosodic processing in schizophrenia. Biological Psychiatry, 58(1), 56.

Lenzenweger, M. F., & Dworkin, R. H. (1996). The dimensions of schizophrenia phenomenology. Not one or two, at least three, perhaps four. British Journal of Psychiatry, 168(APR.), 432.

Lezak, M. D. (1995). Neuropsychological assessment (third ed.). New York: Oxford University Press.

Lieberman, M. D. (2000). Intuition: A social cognitive neuroscience approach. Psychological Bulletin, 126(1), 109-136.

Loughland, C. M., Williams, L. M., & Harris, A. W. (2004). Visual scanpath dysfunction in first-degree relatives of schizophrenia probands: Evidence for a vulnerability marker? Schizophrenia Research, 67(1), 11-21.

Mandal, M. K., Jain, A., Haque-Nizamie, S., Weiss, U., & Schneider, F. (1999). Generality and specificity of emotion-recognition deficit in schizophrenic patients with positive and negative symptoms. Psychiatry Research, 87(1), 39.

Mandal, M. K., Pandey, R., & Prasad, A. B. (1998). Facial expressions of emotions and schizophrenia: A review. Schizophrenia Bulletin, 24(3), 399-412.

Martin, F., Baudouin, J. Y., Tiberghien, G., & Franck, N. (2005). Processing emotional expression and facial identity in schizophrenia. Psychiatry Research, 134(1), 43.

McClure, E. B. (2000). A meta-analytic review of sex differences in facial expression processing and their development in infants, children, and adolescents. Psychological Bulletin, 126(3), 424-453.

Mitelman, S. A., Shihabuddin, L., Brickman, A. M., Hazlett, E. A., & Buchsbaum, M. S. (2005). Volume of the cingulate and outcome in schizophrenia. Schizophrenia Research, 72(2-3), 91.

Perrett, D. I. (1999). A cellular basis for reading minds from faces and actions. In M. Hauser & M. Konishi (Eds.), The design of animal communication. Cambridge, MA: The MIT Press.

Pinkham, A. E., Penn, D. L., Perkins, D. O., & Lieberman, J. (2003). Implications for the neural basis of social cognition for the study of schizophrenia. American Journal of Psychiatry, 160(5), 815-824.

Rajarethinam, R. P., DeQuardo, J. R., Nalepa, R., & Tandon, R. (2000). Superior temporal gyrus in schizophrenia: A volumetric magnetic resonance imaging study. Schizophrenia Research, 41(2), 303-312.

Raven, J. C., Raven, J., & Court, J. H. (1993). Manual for raven's progressive matrices and vocabulary scales. Oxford: Oxford Psychologist Press.

Russell, T. A., Reynaud, E., Herba, C., Morris, R., & Corcoran, R. (2006). Do you see what i see? Interpretations of intentional movement in schizophrenia. Schizophrenia Research, 81(1), 101.

Schmand, B., Bakker, D., Saan, R., & Louman, J. (1991). [the dutch reading test for adults: A measure of premorbid intelligence level]. Tijdschrift voor Gerontologie en Geriatrie, 22(1), 15-19.

Schneider, F., Gur, R. C., Gur, R. E., & Shtasel, D. L. (1995). Emotional processing in schizophrenia: Neurobehavioral probes in relation to psychopathology. Schizophrenia Research, 17(1), 67-75.

Scholten, M. R. M., Aleman, A., Montagne, B., & Kahn, R. S. (2005). Schizophrenia and processing of facial emotions: Sex matters. Schizophrenia Research, 78(1), 61.

Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., et al. (1998). The mini-international neuropsychiatric interview (m.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for dsm-iv and icd-10. Journal of Clinical Psychiatry, 59 Suppl 20, 22-33;quiz 34-57.

Shen, D., Liu, D., Liu, H., Clasen, L., Giedd, J., & Davatzikos, C. (2004). Automated morphometric study of brain variation in xxy males. Neuroimage, 23(2), 648-653.

Shenton, M. E., Dickey, C. C., Frumin, M., & McCarley, R. W. (2001). A review of mri findings in schizophrenia. Schizophrenia Research, 49(1-2), 1-52.

Siegal, M., & Varley, R. (2002). Neural systems involved in 'theory of mind'. Nature Reviews Neuroscience, 3(6), 463.

Sitskoorn, M., Aleman, A., Ebisch, S., Appels, M., & Kahn, R. S. (2003). Meta-analysis of neurocognitive deficits in relatives of patients with schizophrenia: Evidence for a strong cognitive endophenotypic marker. Schizophrenia Research, 60(1), 90-90.

Skuse, D. H. (2005). X-linked genes and mental functioning. Hum Mol Genet, 14 Spec No 1, R27-32.

Takahashi, H., Koeda, M., Oda, K., Matsuda, T., Matsushima, E., Matsuura, M., et al. (2004). An fmri study of differential neural response to affective pictures in schizophrenia. Neuroimage, 22(3), 1247-1254.

Toomey, R., Seidman, L. J., Lyons, M. J., Faraone, S. V., & Tsuang, M. T. (1999). Poor perception of nonverbal social-emotional cues in relatives of schizophrenic patients. Schizophrenia Research, 40(2), 121-130.

Van Der Does, A. J. W., Dingemans, P. M. A. J., Linszen, D. H., Nugter, M. A., & Scholte, W. F. (1996). Symptoms, cognitive and social functioning in recent-onset schizophrenia: A longitudinal study. Schizophrenia Research, 19(1), 61.

Van Rijn, S., Aleman, A., Swaab, H., & Kahn, R. (2006a). Klinefelter's syndrome (karyotype 47,xxy) and schizophrenia-spectrum pathology. British Journal of Psychiatry, 189(5), 459-461.

Van Rijn, S., Aleman, A., Swaab, H., & Kahn, R. S. (2005). Neurobiology of emotion and high risk for schizophrenia: Role of the amygdala and the x-chromosome. Neuroscience and Biobehavioral Reviews, 29(3), 385-397.

van Rijn, S., Swaab, H., Aleman, A., & Kahn, R. S. (2006b). X chromosomal effects on social cognitive processing and emotion regulation: A study with klinefelter men (47,xxy). Schizophrenia Research, 84(2-3), 194-203.

Walker, E. F. (1994). Developmentally moderated expressions of the neuropathology underlying schizophrenia. Schizophrenia Bulletin, 20(3), 453-480.