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ORIGINAL PAPER

Subtle deficits of cognitive theory of mind in unaffected first-degree relatives of schizophrenia patients

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Abstract Alterations of theory of mind (ToM) and empathy were implicated in the formation of psychotic experiences, and deficits in psychosocial functioning of schizophrenia patients. Inspired by concepts of neurocognitive endophenotypes, the existence of a distinct, potentially neurobiologically based social-cognitive vulnerability marker for schizophrenia is a matter of ongoing debate. The fact that previous research on social-cognitive deficits in individuals at risk yielded contradictory results may partly be due to an insufficient differentiation between qualitative aspects of ToM. Thirty-four unaffected first-degree relatives of schizophrenia patients (21 parents, 8 siblings, 5 children; f/m: 30/4; mean age: 48.1 ± 12.7 years) and 34 controls subjects (f/m: 25/9; mean age: 45.9 ± 10.9 years) completed the 'Movie for the Assessment of Social Cognition'—a video-based ToM test—and an empathy questionnaire (Interpersonal Reactivity Index, IRI). Outcome parameters comprised (1) 'cognitive' versus 'emotional' ToM, (2) error counts representing 'undermentalizing' versus 'overmentalizing', (3) empathic abilities and (4) non-social neurocognition. MANCOVA showed impairments in cognitive but not emotional ToM in the relatives' group, when age, gender and neurocognition were controlled for. Relatives showed elevated error counts for 'undermentalizing' but not for 'overmentalizing'. No alterations were detected in self-rated dimensions of empathy. Of all measures of ToM and empathy, only the IRI subscale 'fantasy' was associated with measures of psychotic risk, i.e. a history of subclinical delusional ideation. The present study confirmed subtle deficits in cognitive, but not emotional ToM in first-degree relatives of schizophrenia patients, which were not explained by global cognitive deficits. Findings corroborate the assumption of distinct social-cognitive abilities as an intermediate phenotype for schizophrenia.

Keywords Endophenotype · Theory of mind · Empathy · Movie for the Assessment of Social Cognition (MASC) · Interpersonal Reactivity Index

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Introduction

Theory of mind (ToM) describes the capacity to attribute mental states like thoughts, beliefs, intentions and feelings to oneself and others [1], whereas empathy requires some degree of affective mental state matching between individuals [2]. Amongst the spectrum of social-cognitive deficits implicated in schizophrenia, ToM has received particular attention [3–5]. A substantial body of literature illustrates the importance of ToM for the current understanding of the disease [6], for its functional outcome [4, 7] and targeted therapy [8, 9]. Moreover, as ToM functioning

has been hypothesized to play a crucial role in the pathogenesis of psychotic symptoms [10], the question was raised whether it represents a distinct trait-marker for schizophrenia [11]. Whereas several non-social neurocognitive endophenotypes have been considered in schizophrenia [12–17], the existence of a neurobiologically based social-cognitive vulnerability marker is still a matter of debate [18].

As for ToM, one prospective study demonstrated deficits in perspective-taking as a possible risk marker among children who later developed a schizophrenia spectrum disorder [19]. ToM deficits have been demonstrated in children with schizophrenia [20], in ultra-high-risk individuals [21] and in schizotypy [22, 23]. Studies in remitted schizophrenic patients yielded equivocal results, reporting abnormal as well as unimpaired ToM [24–28]. Previous findings of ToM deficits in unaffected first-degree relatives also support assumptions of a social-cognitive intermediate phenotype for schizophrenia [29–31]. However, these studies have been questioned by conflicting evidence [32–34].

Both in patients and in individuals at genetic risk, mentalizing abilities seem to be related to and to interfere with the expression of psychotic symptoms or schizotypal traits [35–37]. Moreover, the relation of ToM and general cognitive function as well as the pattern of impairment of cognitive versus emotional ToM is still unclear [38]. A differentiation of mentalizing strategies, like excessive ('overmentalizing') versus incorrect or concrete interpretations of others' mental states ('undermentalizing') that both occur in manifest schizophrenia [6, 39], may shed light on the nature of psychosis proneness [40]. However, studies in relatives and at-risk individuals have not systematically investigated these aspects of social cognition [41].

The current study aims to determine differences in social-cognitive function reflecting a putative intermediate phenotype in unaffected first-degree relatives compared with controls. The use of the Movie for the Assessment of Social Cognition (MASC [42]) simultaneously allows to examine the quality of false responses with respect to 'over'—and 'undermentalizing' and to distinguish between cognitive and emotional ToM. Results of ToM testing will be controlled for general neurocognition and compared with subjective data on dispositional empathic abilities and perspective-taking as measured by a self-rating questionnaire (Interpersonal Reactivity Index; IRI [43]). Social cognition in relatives will also be investigated with respect to schizotypal characteristics and individual risk for psychotic disorder.

It was hypothesized that unaffected first-degree relatives of schizophrenic patients would exhibit at least subtle impairments in those dimensions of ToM and empathy that were previously found abnormal in schizophrenia patients [39, 44]. These alterations were assumed to be independent from general neurocognition and from measures of individual risk of psychosis.

Methods

Participants

The study was approved by the local ethics committee; subjects gave written informed consent. Thirty-four unaffected first-degree relatives of patients with diagnosed schizophrenia (DSM-IV) were recruited from the Department of Psychiatry, Charité Universitätsmedizin Berlin and from self-help organizations (21 parents, 8 siblings, 5 children). Participants had no lifetime evidence of psychotic disorder according to DSM-IV and no lifetime exposure to antipsychotic medication. Diagnoses of family members with paranoid schizophrenia were confirmed by medical records. Healthy controls ($n = 34$) matched according to age, educational level and verbal intelligence were recruited by newspaper advertisements. Exclusion criteria for the two groups were DSM-IV axis-I and axis-II disorders. Participants were screened with a structured interview (SKID I/II [45]). Controls reporting mental disorders in their first-degree relatives were also excluded.

Prodromal and attenuated positive symptoms in relatives were assessed using the Scale of Prodromal Symptoms (SOPS/SIPS [46]). All structured interviews were performed by a trained psychiatrist. None of the relatives was prodromal at the time of testing according to the following criteria [47]:

(a) attenuated positive psychotic symptoms with a frequency of several times a week for at least 1 week (APS); (b) Brief limited intermittent psychotic symptoms that last less than 1 week (BLIPS): and (c) a genetic risk with a functional decline during the past year.

Measures

The Movie for Assessment of Social Cognition (MASC) is a video-based test for the evaluation of subtle mindreading difficulties. Test development and validation in patients with Asperger individuals and controls are reported in [42]. The MASC showed the highest sensitivity compared with standard tests of social cognition and a satisfactory internal consistency and test–retest reliability. Test administration requires watching a short film of four people spending an evening together. Participants are instructed to try to understand the characters' mental states and to answer 45 multiple choice questions at given breaks. Questions mostly refer to complex and ambiguous mental states [42].

Correct answers are presented together with 3 distractors corresponding to three types of errors in mental state reasoning tasks. Questions and multiple choice answers are read aloud by the instructor and silently by the participant. Beside a 'sum score' for mental state decoding questions, the MASC categories in detail are the following:

Mental state modalities are reflected by the factors (1) cognitive ('What is X thinking/intending?'; 23 items) and (2) emotional ('What is X feeling?'; 18 items) mental state decoding.

Error categories: Distractors were modelled on the basis of incorrect answers given by participants of the validation sample [42]. Categories are: (1). 'undermentalizing' with two forms (insufficient mental state reasoning indicating incorrect ToM or a complete lack of a mental state concept) and (2) 'overmentalizing' (excessive, over-interpretative ToM).

General cognitive function: A multiple choice vocabulary test (Mehrfachwahlwortschatztest, MWT-B [48]) was applied to estimate verbal intelligence. The Auditory Verbal Learning Test (AVLT [49]) served as a measure of multiple verbal memory components. For statistics, mean scores of the five initial presentations ($AVLT^{(1-5)}$) were used for short-term memory, verbal learning and prefrontal control of mnemonic strategies as well as scores for pro-active interference ($AVLT^{(pro)}$) as an indicator of executive function.

The Interpersonal Reactivity Index (IRI [43]) assesses four aspects of empathic responding, which were determined by factor analysis. We used the German translation ('Saarbrücker Persönlichkeitsfragebogen' [50]). The original four 7-item-subscales were answered in a 5-point Likert scale: 'Perspective taking' (PT) refers to the tendency to spontaneously adopt the psychological point of view of others and to reason about their mental states. The 'empathic concern' (EC) scale comprises respondents' prosocial feelings of warmth, compassion and concern for others. 'Personal distress' (PD) measures self-oriented feelings of anxiety and discomfort in response to the distress of others. The fourth subscale 'fantasy' (FS) taps the tendency to identify with fictitious characters in books and movies. Construct validity of the IRI scales was supported in several studies (Davis [43]).

The *Schizotypal Personality Questionnaire* (SPQ [51]; German version [52]) was used to assess schizotypy in relatives. Besides the total score, three subscores were calculated: cognitive-perceptual (SPQ-CP: ideas of reference, magical thinking, unusual perceptual experiences, suspiciousness), social-interpersonal (SPQ-SI: social anxiety, no close friends, constricted affect) and disorganization score (SPQ-D: eccentric behaviour, eccentric speech) [53, 54].

The *Peters Delusions Inventory* (PDI [55]) was used in the relatives group to estimate the life-time occurrence of subthreshold delusional symptoms.

Statistical calculations were carried out as indicated in the results section using PASW Statistics 18®. Effect sizes were estimated as η^2 based on PASW output; *f*-values were calculated using G*power [56]. Statistical significance was defined at a 2-sided $P < 0.05$. Control for Type I error was performed according to Bonferroni–Holm [57].

Results

Demographic and neuropsychological data are given in Table 1. Relatives and healthy controls did not differ significantly in age, gender, verbal intelligence, years of

Table 1 Demographic and neuropsychological data in first-degree relatives of schizophrenic patients and controls; between-group comparisons: *T*-test for independent samples (two-sided)

	First-degree relatives ($n = 34$)	Healthy controls ($n = 34$)	Statistics
Age (mean years ± SD)	48.1 ± 12.7	45.9 ± 10.9	$T = 0.74$, $P = 0.46$
Gender (f/m)	30/4	25/9	NS[a]
Education (mean years ± SD)	16.0 ± 3.1	15.5 ± 2.4	$T = 0.80$, $P = 0.44$
IQ (MWT-B) (mean ± SD)	117.8 ± 13.4	115.5 ± 11.6	$T = 0.76$, $P = 0.45$
$AVLT^{(1-5)}$ (mean ± SD)	11.4 ± 1.6	10.6 ± 1.7	$T = 1.89$, $P = 0.06$
$AVLT^{(pro)}$ (mean ± SD)	11.4 ± 2.6	10.2 ± 2.7	$T = 1.64$, $P = 0.10$
MASC 'overmentalizing'	4.7 ± 2.9	4.7 ± 1.9	$T = -0.10$, $P = 0.93$
MASC 'undermentalizing'	8.2 ± 4.3	6.3 ± 3.1	**$T = -2.10$, $P = 0.04$**
MASC cognitive mental states	16.1 ± 2.9	17.8 ± 2.0	**$T = 2.78$, $P = 0.01$**
MASC emotional mental states	13.2 ± 2.4	13.8 ± 2.0	$T = 1.06$, $P = 0.29$
IRI perspective-taking	26.2 ± 4.4	25.1 ± 3.9	$T = -1.05$, $P = 0.30$
IRI empathic concern	27.1 ± 4.0	25.3 ± 3.8	$T = -1.87$, $P = 0.07$
IRI personal distress	18.1 ± 3.9	16.7 ± 4.8	$T = -1.30$, $P = 0.20$
IRI fantasy	23.3 ± 4.6	23.6 ± 4.4	$T = 0.29$, $P = 0.77$

Significant results indicated in *bold* type

[a] χ^2-Test

Table 2 Assessment of psychotic risk in first-degree relatives: Schizotypal Personality Questionnaire (SPQ) sum score and subscales; Peters Delusions Inventory (PDI)

($n = 34$)	SPQ-sum	SPQ-CP	SPQ-D	SPQ-SI	PDI
Mean score ± SD	9.1 ± 6.6	3.7 ± 3.6	2.1 ± 1.9	3.3 ± 3.1	3.9 ± 4.2
Median	7.5	3.0	2.0	3.0	2.5
Range	0–24	0–15	0–7	0–14	0–14

SPQ-CP cognitive-perceptual, *SPQ-SI* social-interpersonal, *SPQ-D* disorganization

education and AVLT. None of the relatives was found to currently exhibit manifest or subthreshold psychotic symptoms according SIPS/SOPS interview and PDI (Table 2). PDI and SPQ total and subscores are given in Table 2. Taken together, symptom load of relatives was low.

Movie for the Assessment of Social Cognition

A MANCOVA was performed with MASC cognitive and emotional mental state decoding as dependents, status (relative/control) and gender as fixed factors, and age, verbal IQ, $AVLT^{(pro)}$ and $AVLT^{(1–5)}$ as covariates. Relatives and controls differed significantly in MASC cognitive, but not in MASC emotional mental state decoding (Fig. 1). Effect sizes were $\eta^2 = 0.083$ ($f = 0.30$) for MASC cognitive and $\eta^2 = 0.045$ ($f = 0.22$) for MASC emotional mentalizing; $f = 0.25$ being considered a moderate effect. Both conditions were associated with age (cognitive mentalizing: $\eta^2 = 0.069$; $f = 0.27$; emotional mentalizing: $\eta^2 = 0.11$; $f = 0.35$), but not with gender, verbal IQ and memory; one exception being the interrelation of the $AVLT^{(1–5)}$ and emotional mental state decoding ($\eta^2 = 0.079$; $f = 0.29$). MASC emotional mentalizing was significantly related to short-term memory ($AVLT^{(1–5)}$) in the relatives' group (r[Pearson] = 0.63, $P < 0.001$), but only by trend in the control group (r[Pearson] = 0.34, $P = 0.05$).

A second MANCOVA was conducted with MASC 'overmentalizing' and 'undermentalizing' scores as dependent variables and the same set of factors and covariates. Relatives showed more error responses indicating a tendency towards 'undermentalizing', when controlled for age, gender and verbal intelligence, which all also had significant differential impact on the dependent variables (Table 3).

Interpersonal Reactivity Index

As for self-rated dimensions of empathy, MANCOVA showed a statistically significant overall difference between relatives and controls, when age, verbal IQ and memory were controlled for. However, between-subject

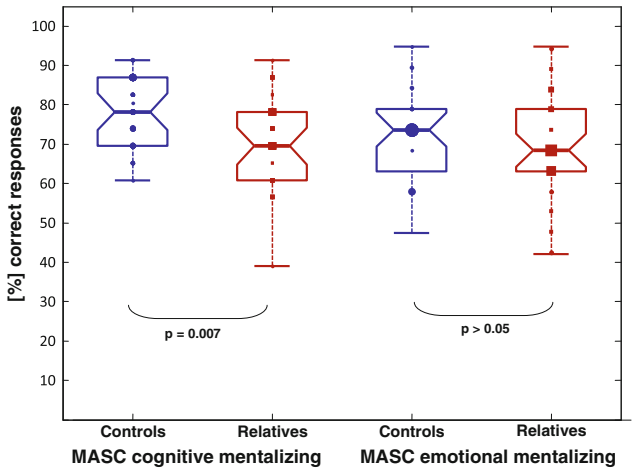

Fig. 1 MASC cognitive and emotional mentalizing scores in first-degree relatives and controls ($n = 34/34$; *boxplot*: medians, interquartile range, *whiskers*: interquartile range × 1.5, *notches*: variability of the median between samples with $P < 0.05$; marker size proportional to number of values; between-group comparisons: *T*-test for independent samples)

analysis revealed no significant differential effects of status as a relative on the four dependent variables. IRI subscore 'fantasy' displayed a robust relation with verbal IQ and executive functioning—interestingly, this could not be shown for the other IRI factors, e.g. perspective taking (Table 4).

There was no significant correlation between MASC and IRI outcome parameters in the relatives' sample.

Psychotic risk, MASC and IRI scores in the relatives' group:

In order to determine the impact of psychotic risk as determined by schizotypy and history of subthreshold psychotic symptoms within the relatives group, we performed a correlational analysis of MASC and IRI parameters with sum scores of PDI and SPQ. Significant positive correlations were found between the IRI subscale 'fantasy' and the PDI sum score (r[Spearman] = 0.58, $P < 0.001$) as well as IRI subscale 'personal distress' and PDI sum score (r[Spearman] = 0.35, $P = 0.041$), the latter being

Table 3 Theory of mind in first-degree relatives of schizophrenia patients and controls: MANCOVAs and post hoc ANOVAs with subscores of the Movie for the Assessment of Social Cognition (MASC) as dependent variables: MANCOVA 1: cognitive and emotional ToM; MANCOVA 2: undermentalizing and overmentalizing

	Factors		Covariates			
	Status	Gender	Age	AVLT$^{(1-5)}$	AVLT$^{(pro)}$	Verbal IQ
MANCOVA 1 F[2,61]	**3.69***	0.27	**5.26****	**4.00***	0.58	0.47
Post hoc ANOVA F[1,62]						
Cognitive mental states ($R^2_{adj} = 0.17$)	**6.10****	0.05	**5.10***	0.18	1.18	0.00
Emotional mental states ($R^2_{adj} = 0.32$)	3.67	0.54	**8.80****	**6.43****	0.16	0.88
MANCOVA 2 F[2,61]	2.99	3.09	**5.88****	1.22	0.53	**3.40***
Post hoc ANOVA F[1,62]						
Undermentalizing ($R^2_{adj} = 0.24$)	**4.91***	0.66	**11.32****	0.34	0.54	**4.55***
Overmentalizing ($R^2_{adj} = 0.12$)	0.36	**6.19****	0.01	1.72	0.76	**3.79***

Factors: status as a relative or control, gender, age; covariates: age, verbal IQ, AVLT$^{(1-5)}$: short-term verbal memory/learning, AVLT$^{(pro)}$: resistance to interference. Significant results are indicated in *bold* type (* $P < 0.05$, ** $P < 0.01$)

Table 4 Self-rated dimensions of empathy in first-degree relatives of schizophrenia patients and controls: MANCOVA and post hoc ANOVAs with subscales of the Interpersonal Reactivity Index (IRI) as dependent variables

	Factors		Covariates			
	Status	Gender	Age	AVLT$^{(1-5)}$	AVLT$^{(pro)}$	Verbal IQ
MANCOVA 3 F[4,59]	**2.70***	1.16	2.36	0.97	**5.52*****	**4.48****
Post hoc ANOVA F[1,62]						
Fantasy $R^2_{adj} = 0.22$	0.81	0.87	3.10	0.47	**5.04***	**18.43*****
Empathic concern $R^2_{adj} = -0.01$	3.37	0.02	0.13	1.43	1.21	0.38
Perspective taking $R^2_{adj} = 0.04$	2.54	3.17	2.53	2.01	1.43	1.32
Personal distress $R^2_{adj} = 0.06$	1.63	1.46	3.90	0.19	0.88	0.05

Factors: status as a relative or control, gender, age; covariates: age, verbal IQ, AVLT$^{(1-5)}$: short-term verbal memory/learning, AVLT$^{(pro)}$: resistance to interference. Significant results are indicated in *bold* type (* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$)

not maintained after alpha-level-adjustment. There were no significant associations between MASC 'cognitive' and 'emotional mental state' attribution and risk markers. With respect to the problem of multiple comparisons and the lack of significant correlations of the SPQ-sum score, we abstained from assessing SPQ subscores separately.

Discussion

Theory of mind (ToM) and empathy have been proposed as candidate endophenotypes for schizophrenia [11]. However, compared with the abundance of studies investigating non-social-cognitive endophenotypes, research concerning social-cognitive trait-markers is in its early stages [18]. The present study investigated social cognition in unaffected first-degree relatives of patients with schizophrenia compared with controls, using an experimental setting that allows a simultaneous evaluation of cognitive and emotional ToM as well as of different mentalizing strategies. Results were related to factors of general cognition, pychopathology and self-rated dimensions of empathy.

Cognitive and emotional ToM

Unaffected individuals at familial risk in our sample showed significantly lower MASC cognitive ToM scores than controls. There were no significant differences in MASC emotional ToM. Corroborating existing evidence for ToM impairments in unaffected relatives of schizophrenic patients [11], our data suggest that subtle differences in cognitive ToM might be associated with genetic liability to schizophrenia. Contrastingly, no significant group differences were detected for emotional ToM. To our knowledge, there have been no studies trying to dissect cognitive and emotional ToM in a combined experimental design in 'at risk' individuals to date. Of note, patients with paranoid schizophrenia were shown to exhibit robust

impairments in MASC cognitive and also emotional ToM [39], whereas deficits of euthymic patients with bipolar disorder were also restricted to the cognitive realm [58]. Our findings are in unison with investigations reporting altered cognitive ToM [25, 29, 36, 37, 59] and studies demonstrating unimpaired emotional ToM on the Eyes Test [32] or normal emotion perception [60] in individuals 'at risk'. However, other studies reported controversial findings, like impaired facial emotion recognition [61–64] or altered emotional mental state inference from photographs depicting the eye region [30, 31]. Moreover, de Achával et al. [30] found deficits of relatives in the faux-pas-test that requires attribution of emotional mental states on the basis of verbal contextual information—however, this result was impacted by memory. Inconsistencies cannot easily be explained by differences in task difficulty. MASC emotional items demand the attribution of more complex emotional mental states and require considering all affective dispositions of a character in order to identify his/her correct emotion. Our result on the one hand suggests a preservation of emotional mentalizing in unaffected relatives. On the other hand, the provision of situational context may also have alleviated problems with basic emotion recognition or vice versa. Furthermore, it cannot be ruled out that relatives of schizophrenic patients were simply well trained in the detection of subtle emotional signals by the necessity to care for their diseased family members. This effect may play an important role in our sample which was dominated by parents of schizophrenic patients.

'Overmentalizing' versus 'undermentalizing'

Our results indicate that ToM deficits in relatives might be attributable to 'undermentalizing' and not to an excessive, over-interpretative ascription of mental states ('overmentalizing'). 'Overmentalizing' was suggested to be involved in the formation of acute, delusional symptoms and the interpretation of meaning in randomness [10, 40], while 'undermentalizing' was assumed to be more prominent in patients with negative symptoms, thought disorder and developmental onset of the disease [6]. Unfortunately, most experimental settings in ToM research do not differentiate between types of error responses. Over-attribution of emotions to neutral faces in individuals at genetic risk was shown to be related to positive and prodromal psychopathology [63]. In contrast, our relatives were free of psychotic symptoms, and no correlation was found between mentalizing styles and a history of previous symptoms. This can be interpreted in favour of state dependence of 'overmentalizing', whereas 'undermentalizing' might bear trait characteristics.

Self-rated dimensions of empathy

Using self-rating questionnaires like the IRI in schizophrenia, lower scores for 'perspective taking' as well as higher ratings of 'personal distress' have been demonstrated [44, 65]. In contrast to our expectations, no significant differences in the four dimensions of empathy could be detected between relatives and controls in the current study. However, self-ratings in relatives of schizophrenic patients may be affected by the fact that relatives adapted to and reflected their role as carers, leading to higher scores in IRI 'perspective taking', 'empathic concern' and 'personal distress'. This may explain the tendency towards inverse group differences at subjective IRI ratings compared with more objective MASC cognitive scores. Of note, Henry et al. [66] reported a negative correlation between objective performance on the Eyes Test and self-rated cognitive empathy in schizotypal individuals. However, behavioural (MASC) and perceived (IRI) mentalizing skills were not related in our low-schizotypal sample.

Specificity of social-cognitive deficits

Social-cognitive deficits in schizophrenia are confounded by general cognitive dysfunction [67]—this may also apply to studies in high-risk individuals who have been shown to exhibit subclinical non-social-cognitive alterations [15]. In first-degree relatives evidence is scant, as not all ToM studies do control for general cognition [11, 33, 34]. In the present study, relatives and controls were matched according to verbal IQ, and the relatives group scored slightly better than controls in a measure of verbal short-term memory and learning, resistance to interference as well as executive control of mnemonic strategies (AVLT subscores). Verbal IQ and AVLT subscores were introduced as covariates in the analysis, but group differences for MASC cognitive mentalizing remained significant; AVLT performance was not associated with cognitive, but with affective mentalizing. Our findings can be cautiously interpreted in favour of an at least partly independent nature of the ToM deficit in unaffected first-degree relatives. Eack et al. [63] also reported relatively weak relations between social and non-social-cognitive impairments in relatives and suggested a stronger convergence of both deficits in schizophrenia. Of note, our sample of relatives did not contain ultra-high-risk or prodromal individuals, so that the subtle deficit in cognitive mentalizing might indeed reflect a trait-dependent or endophenotypical characteristic of healthy individuals at genetic risk. However, studies looking at both social and non-social cognition in relatives of schizophrenic patients are rare, and further research is warranted with respect to their interrelations.

Schizotypy and history of psychotic experience

Schizotypy and delusion-proneness were investigated in the relatives sample to determine the effect of psychotic risk on ToM performance. No significant correlations were found between MASC ToM and schizotypy scores. This is in line with research reporting the absence of ToM deficits in non-clinical schizotypal populations [36, 40, 68, 69]. However, SPQ mean scores and ranges in the present sample were rather low. Other studies suggest that ToM deficits are restricted to high-schizotypal samples [22, 70]. Also, circumscribed ToM deficits were found to be related to 'positive' schizotypy [23] or high scores of 'magical ideation'[71]. In relatives of schizophrenic patients, ToM deficits were found to be associated with higher levels of SPQ social-interpersonal problems or 'negative' schizotypy [31]. However, because of low variance of schizotypy scores in our sample of relatives and the lack of a significant association with ToM and empathy measures, SPQ subscales were not assessed separately.

Furthermore, there was no significant association between the subthreshold psychotic symptoms in the past with MASC scores in our relatives sample. This is in contrast to findings of ToM deficits in previously symptomatic compared with never-psychotic relatives [72] and the study of Fyfe et al. [40], who reported an association between 'overmentalizing' and high PDI scores in non-clinical subjects. Our findings do not support views of an intrinsic relationship between a psychotic symptoms continuum and a theory of mind impairment in people at risk of schizophrenia, which would confine abnormal ToM to the presence of subclinical symptoms [41].

In contrast, significant associations appeared between the IRI subscale 'fantasy'—the disposition to identify with fictional characters—and life-time subthreshold delusional experiences in the relatives group. Our results are consistent with the view that 'fantasy' converges with delusion-proneness, cognitive-perceptual aberrations and disorganized features [73]. Pronounced 'fantasy' may indicate some vulnerability for schizophrenia [74], but might represent a reasoning style like cognitive slippage or perceptual immersion that is normally distributed in the population and pronounced in at-risk populations, and but has to interact with attributional biases in order to result in psychosis [75]. However, 'fantasy' was questioned to represent an aspect of cognitive empathy but was rather related to emotionality [76], suggestibility, dissociative experiences [77, 78] or constructs like 'transliminality' [79]. Supported by the lack of an association with SPQ scores, 'fantasy' may represent a style of reasoning independent from schizotypal features in our sample. However, these findings need replication in independent studies and warrant further research. As always, correlational analyses have to be interpreted with caution.

Limitations

Several limitations of our study have to be discussed, the most important of which refers to the modest sample size ($n = 2 \times 34$). Therefore, it cannot be excluded that the present pattern of mentalizing deficits in first-degree relatives is a result of insufficient statistical power. Although significant, the effect size of the reported association between MASC cognitive mentalizing and diagnostic group was only moderate [80]. Results should therefore interpreted with caution. On the other hand, diagnostic group compared with other independents explained a comparably large part of the variance of ToM parameters in our sample. Moreover, the predominance of parents did not allow for subanalyses with respect to a differentiation of parents, siblings or children of schizophrenic patients. This fact also limited the possibility to explore the role of other variables such as differences in genetic load, i.e. multiplex versus simplex families [81]. Due to the heterogeneity of the present sample, data have to be interpreted with caution, in particular when comparing with results from differently composed samples. Moreover, males and females were shown to rely on somewhat different neural networks when processing empathic stimuli [82, 83], and there is some indication for a higher performance of females at ToM and empathy tests [84, 85]. Nevertheless, no sex differences were found as for MASC performance in schizophrenia and healthy controls [39]. However, the predominance of females in our sample may explain normal emotional ToM of first-degree relatives in our study compared with previous research [30, 31]. Moreover, the mean age of our sample was well beyond the main manifestation period of schizophrenic psychoses and may have led to a selection of individuals at lower clinical risk. The exclusive use of the MASC as a ToM test poses another limitation of the study. Strengths of the MASC are the simultaneous investigation of cognitive and emotional ToM as well as 'undermentalizing' and 'overmentalizing' in a relatively naturalistic experimental setting. Relatives and controls were well-matched with respect to IQ, years of education and age, and all analyses were controlled for the impact of non-social cognition. However, actual social function and involvement in the care of schizophrenic family members were not assessed, so that other moderating circumstances can play a role [86]. Further research should include schizophrenic patients and their relatives as well as control families as homogeneous trios [29], strive for longitudinal designs and integrate genetic and neurobiological parameters.

Conclusion

The main finding of our study is the occurrence of subtle alterations of cognitive, but not emotional ToM in first-degree relatives of schizophrenic patients, which cannot be attributed to impairments in basic non-social neurocognitive function. ToM deficits were due to 'undermentalizing', while the extent of 'overmentalizing' was comparable to controls—a result which may corroborate the assumption of selected social-cognitive abilities as putative endophenotypes for schizophrenia. The clinical significance of our findings lies in the field of targeted preventative interventions which therapeutically target the cognitive aspects of ToM in non-clinical individuals with a genetic risk of schizophrenia.

Conflict of interest None.

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