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Familial covariation of facial emotion recognition and IQ in schizophrenia

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Abstract
Alterations in general intellectual ability and social cognition in schizophrenia are core features of the disorder, evident at the illness’ onset and persistent throughout its course. However, previous studies examining cognitive alterations in siblings discordant for schizophrenia yielded inconsistent results. Present study aimed to investigate the nature of the association between facial emotion recognition and general IQ by applying genetically sensitive cross-trait cross-sibling design. Participants (total \(n=158\); patients, unaffected siblings, controls) were assessed using the Benton Facial Recognition Test, the Degraded Facial Affect Recognition Task (DFAR) and the Wechsler Adult Intelligence Scale-III. Patients had lower IQ and altered facial emotion recognition in comparison to other groups. Healthy siblings and controls did not significantly differ in IQ and DFAR performance, but siblings exhibited intermediate angry
facial expression recognition. Cross-trait within-subject analyses showed significant associations between overall DFAR performance and IQ in all participants. Within-trait cross-sibling analyses found significant associations between patients’ and siblings’ IQ and overall DFAR performance, suggesting their familial clustering. Finally, cross-trait cross-sibling analyses revealed familial covariation of facial emotion recognition and IQ in siblings discordant for schizophrenia, further indicating their familial etiology. Both traits are important phenotypes for genetic studies and potential early clinical markers of schizophrenia-spectrum disorders.

**Keywords:** cognitive alterations; schizophrenia families; cross-trait cross-sibling design;

1. Introduction

   Cognitive alterations (i.e. alterations in general intellectual ability and social cognition) seen in patients with schizophrenia are now recognized as a core feature of the disorder (Billeke and Aboitiz, 2013; Cannon et al., 2000; Elvevag and Goldberg, 2000). Not specific to the illness’ subtypes, they are evident at the onset of the illness (in unmedicated patients), largely state-independent and persistent in a trait-like fashion, thus potentially reflecting a genetic liability to schizophrenia-spectrum disorders.

   The neurodevelopmental hypothesis proposes that cognitive alterations, which may represent altered brain development resulting from gene-environment interactions, are likely to emerge during childhood/adolescence and to precede full-blown psychosis (Marenco and Weinberger, 2000). It is well known that most pre-schizophrenia subjects fail to reach their
expected level of general cognitive ability during childhood (Jones et al., 1994) and that general IQ alterations characterize a majority of schizophrenia patients throughout the lifespan (Bilder et al., 2006; Kremen et al., 2001). Likewise, facial emotion recognition impairment has been reported early in the course of schizophrenia, and it is believed to generalize across emotional valences with the illness progression (Addington et al., 2006; Kohler et al., 2010).

Although social cognition requires general cognitive capacities and there may be some functional overlap of brain areas underlying social cognition and other more general cognitive processes, previous evidence have shown that aforementioned cognitive domains are distinct from one another and that social cognitive impairments in schizophrenia are separable from the general cognitive ability (Allen et al., 2007; Sergi et al., 2007). Neuroimaging and lesion studies have shown that social tasks activate specific brain areas that can be distinguished from those activated by non-social tasks, for example superior temporal sulcus, medial prefrontal cortex (Adolphs, 2001; Harris et al., 2005; Mitchell et al., 2004), amygdala, fusiform gyrus and insular regions (Bar-On R et al., 2003). Consecutively, the MATRICS-NIMH consensus cognitive battery for schizophrenia categorized social cognition as one of the seven major separate cognitive domains that are altered in schizophrenia, alongside with: Speed of Processing, Attention/vigilance, Working Memory, Verbal Learning and Memory, Visual learning and Memory and Reasoning and Problem Solving (Green et al., 2004).

Since it has been shown that some of the healthy siblings of patients with schizophrenia also exhibit certain cognitive alterations (i.e. alterations in general IQ and facial emotion recognition), it has been proposed that aforementioned cognitive changes might represent indicators of vulnerability to schizophrenia-spectrum disorders, deriving from primarily genetic (and/or shared environmental) etiologic influences (Cannon et al., 2000; Lavoie et al., 2013).
However, previous studies examining cognitive alterations in siblings discordant for schizophrenia yielded inconsistent results, and the degree to which these alterations co-segregate in schizophrenia-spectrum families have yet to be further investigated.

Many first degree relatives of schizophrenia patients are predisposing genotype carriers without manifesting the disorder phenotypically. Sibling status represents an indirect measure of genetic risk since the risk for schizophrenia in those individuals is increased 5- to 10-fold, and twin studies have shown that familial clustering is mainly due to genetic factors (Sullivan et al., 2003). Research in those individuals, deemed to be at different level of genetic risk for psychosis, could provide better insight to the pathogenesis of the illness and to indicate potential targets for preventive treatments. Thus, it might be worthy investigating familial covariation of alterations in general IQ and emotion recognition performance. Both phenotypes have been shown to cluster within families, but the nature of the aforementioned relationships is still insufficiently evaluated and clarified. It might reflect a shared familiar etiology with a possible genetic basis. Alternatively, both IQ and emotion recognition performance might be on a common causal pathway or secondary to another factor.

The present study aimed to investigate whether a shared familial liability may underlie the association between facial emotion recognition alteration and general IQ alteration by applying genetically sensitive cross-trait cross-sibling design (previously described by GROUP investigators Fett et al. (2013) and Latater et al. (2012)) in a sample comprised of three groups of participants with decreasing levels of familial schizophrenia liability (patients, their unaffected siblings, healthy controls). Cross-trait cross-sibling analyses allow investigation of an etiological association between (subclinical level of expression of) two phenotypes, while removing the effects of illness-related factors, such as residual symptoms and medications.
At the first step, we explored facial emotion recognition performance and general IQ in schizophrenia probands and their unaffected siblings compared to controls. Next step was the analysis of the association between facial emotion recognition and general IQ within patient and sibling group (cross-trait within subject analysis), to confirm the assumption of the overlap between aforementioned domains. Furthermore, we explored familial clustering of general IQ and facial emotion recognition performance (within-trait cross-sibling analysis). Finally, we explored the associations between patients’ facial emotion recognition performance and siblings’ general IQ, and between patients’ IQ and their siblings’ facial emotion recognition ability (cross-trait cross-sibling analyses). The presence of such associations would be indicative of a shared familial etiology of both traits, while finding of associations within patients only would suggest that the overlap between lower IQ and impaired facial emotion recognition was rather due to the individual factors (i.e. secondary to illness related effects).

2. Methods

2.1. Sample and procedure

Present sample comprised 158 participants originating from Belgrade and surroundings catchment area: 52 patients with schizophrenia-spectrum disorders, 55 of their unaffected siblings and 51 healthy controls. Patients were recruited from regional mental health institutions, unaffected siblings were recruited through participating patients, while control group was randomly recruited from the catchment area via local marketing agency. Inclusion criteria for all participants were: age ≥ 18 years, IQ ≥ 70, normal vision (or corrected to normal), no recent history of alcohol or drug abuse, being able and willing to give informed consent. Patients had to meet DSM-IV criteria for psychotic disorder as assessed by Mini International Neuropsychiatric Interview (Sheehan et al., 1998), not caused by neurological disorder, currently remitted (GAF
score > 40), whereby the illness duration did not exceed 10 years. Additional inclusion criteria for unaffected siblings of schizophrenia patients and controls were the absence of personal history of psychiatric disorders, and the absence of family history of psychiatric disorders for control group only. The study was conducted in accordance with the Declaration of Helsinki and its design was approved by the Medical Ethics Committee of the School of Medicine, University of Belgrade. All participants gave their written informed consent, and control subjects received compensation (vouchers) for their study participation.

2.2. Measures

The Benton Facial Recognition Test (BFRT) (Benton et al., 1983), an accurate measure of the ability to match non-emotional unfamiliar faces, was used for the assessment of participants’ general facial recognition ability. Participants were simultaneously presented with one target and six other black and white photos of unfamiliar male or female faces with their hair and clothing shaded out. Afterwards, they were asked to: (1) match a frontal view of the target with an identical photo, (2) match a frontal view of the target face with 3 photos taken from different angles, and (3) match a frontal view of the target face with three photos of that person taken under different lighting conditions. Total number of correct answers served as main outcome parameter.

The Degraded Facial Affect Recognition Task (DFAR) (Van ‘t Wout et al., 2004) was used for the assessment of participants’ ability to recognize four basic emotional facial expressions: neutral, happy, fearful and angry. This experimental task consists of 64 face presentations (16 in each emotion category) of two male and two female actors depicting aforementioned emotions. Visual contrast was reduced by 30% in order to enhance the
contribution of interpretation. Main outcome parameters were the percentages of correct answers per each facial expression and the overall percentage of correct answers.

Wechsler Adult Intelligence Scale- III (WAIS-R) (Velthorst et al., 2013). A brief, 15-minute, version of the WAIS scale, comprised of subtests Arithmetic, Digit Symbol Coding, Information and Block Design, was used to assess participants’ general intellectual ability. It has been previously shown that this scale gives reliable estimates of the Full Scale IQ in all three groups of participants (patients with schizophrenia-spectrum disorders, their unaffected siblings and unrelated healthy controls), thus it was proposed as a useful screening device for general intellectual ability in research settings.

Global Assessment of Functioning scale (GAF) (Hall, 1995). Numeric scale (ranging from 0 to 100), designed for the assessment of social and occupational functioning and presence of psychiatric symptoms, was used to confirm current remission.

2.3. Statistical analyses

All statistical analyses were performed using the SPSS version 19 package (Armonk, NY: IBM Corp). Initially, all data were tested for normality (Shapiro-Wilks test), and accordingly analyzed using appropriate parametric or non-parametric tests. Between group differences in socio-demographic characteristics, facial emotion recognition performance and general intellectual ability were assessed using chi-square, Mann-Whitney and student’s t-test. Partial correlation analyses were used to assess the associations between DFAR performance and IQ within all three groups of participants (cross-trait within-subject analyses), familial clustering of IQ and facial emotion recognition performance (within-trait cross-sibling analyses), and associations between patients’ DFAR performance and siblings’ IQ (cross-trait cross-sibling
analyses). As previous research demonstrated that age (Isaacowitz et al., 2007) and gender (Donges et al., 2012) have impact on facial emotion recognition performance, their potential confounding effect was controlled for in all further analyses. Afterwards, all analyses on DFAR performance were adjusted for general facial recognition ability (BFRT). In the cases of families contributing with more than one proband or unaffected sibling, all possible sibling pairs were analyzed.

3. Results:

3.1. Sample characteristics and between-group differences

Main socio-demographic/clinical characteristics and cognitive performance indices of the sample are presented in Table 1. Groups did not differ in terms of age and sex, while significant between-group differences were observed in most cognitive tests. Patients showed significantly lower IQ and poorer performance on BFRT and DFAR tasks than both their siblings and control group. Precisely, in comparison to siblings and controls, schizophrenia patients exhibited impaired overall facial emotion recognition (i.e. DFAR total) and impaired recognition of neutral and fearful facial expression. Furthermore, patients’ showed significantly poorer recognition of angry facial expression than control group only.

Siblings’ angry facial emotion recognition performance did not significantly differ in comparison to other examined groups, but the trend toward significance was evident for both patients and controls, suggesting siblings’ intermediate achievement on this task. Descriptive statistics revealed significant positive trend for the angry facial expression recognition regarding examined groups (when treated as an ordinal variable). However, present sample size was insufficient to reveal significant differences between mean level of angry facial expression
recognition performance of siblings and patients (1-beta= 41.5%), as well as between siblings and controls (1-beta= 33.8%). Significant correlation between groups (in ordered categories) and angry facial expression recognition were observed with positive trend (Rho=0.25, p=0.00) therefore confirming the possible trend of angry facial expression recognition regarding groups. Box plot diagram also revealed positive trend of angry facial expression recognition with regard to groups.

No significant between-group differences in recognizing happy facial expression were observed. Despite patients’ overall facial emotion recognition impairment, the valence-related performance pattern was similar in all three groups of participants. All participants most accurately recognized happy facial expression, followed by neutral, angry and fearful facial expression with the lowest rate of correct answers. No significant differences in general IQ and facial emotion recognition performance were observed between unaffected siblings and controls. Table 2 summarizes between-group differences on the administered cognitive tests.

3.2. Cross-trait within-subject, within-trait cross-sibling and cross-trait cross-sibling analyses

Table 3 presents all partial correlation analyses (controlled for age and sex) between patients’ and siblings’ general IQ and overall facial emotion recognition performance.

Cross-trait within-subject analyses have revealed significant associations between overall DFAR performance and general intellectual ability in all three groups of participants (i.e. patients, healthy siblings, controls). Unaffected siblings showed the strongest association between aforementioned traits, followed by healthy controls and patients (with the lowest, but significant correlation coefficients). After adjusting for general facial recognition ability (BFRT), correlation between general IQ and overall DFAR performance remained significant in sibling
Furthermore, within-trait cross-sibling analyses have shown significant associations between patients’ and their siblings’ IQ, and between patients’ and siblings’ overall DFAR performance as well. This finding was suggestive of significant clustering of facial emotion recognition ability and general IQ within families of patients with schizophrenia-spectrum disorders.

Finally, cross-trait cross-sibling analyses have revealed that patients’ overall facial emotion recognition performance was significantly correlated with their siblings’ general IQ. Moreover, patients’ IQ was also significantly correlated with their siblings’ total DFAR performance. All correlations remained significant even after controlling for patients’ and siblings’ general facial recognition ability (BFRT).

4. Discussion
4.1. Facial emotion recognition ability and general IQ over the schizophrenia-spectrum continuum

The present study demonstrated altered processing of emotional information in patients with schizophrenia-spectrum disorders in comparison to both their unaffected siblings and controls. In line with the earlier evidence related to emotion-specific processing deficits in schizophrenia (Allot et al., 2015; Bediou et al., 2007; Fett et al., 2013), we found impaired recognition of angry and fearful facial expressions (i.e. negative emotional valence) and unimpaired recognition of happy facial expression in the patient group in comparison to sibling and control groups. On the other side, contrary to the majority of previous findings, our patient
group exhibited impaired recognition of neutral facial expression in comparison to both siblings and controls. However, Ruocco et al. (2014) and Kohler et al. (2003) have also reported deficits perceiving neutral faces in patients with schizophrenia-spectrum disorders. Possible explanation for that finding is aberrant assignment of salience to neutral stimuli that was earlier described in psychotic patients (Kapur, 2003). Moreover, studies by Ruocco et al. (2014) and by Eack et al. (2010) have demonstrated that individuals at genetic risk of schizophrenia (i.e. siblings) also tend to have negative attribution bias (i.e. to misinterpret neutral faces as negative), a finding that we did not replicate in our study. Previous studies examining facial emotion recognition in siblings discordant for schizophrenia yielded inconsistent results. Some of them reported subtle but significant difficulties in facial emotion recognition in unaffected siblings of schizophrenia patients (Alfimova et al., 2009; Bediou et al., 2007; Kee et al., 2004), while others have found small and non significant differences relative to healthy controls (Cella et al., 2015; Fett et al., 2013). This variability across studies could be, at least partially, explained by the methodological differences between studies (i.e. characteristics of the study subjects, tasks used to assess facial emotion recognition). In the present study, siblings’ overall facial emotion recognition performance and their ability to recognize fearful and angry facial expressions were somewhat lower, although the differences between siblings and controls were small and non significant. Nevertheless, angry facial expression recognition ability was distributed along a continuum between the patients and controls in our study, with the unaffected siblings showing intermediate achievement.

A similar pattern of achievement was observed for general cognitive ability. Patients’ general IQ was significantly lower in comparison to their unaffected siblings and controls.
Suggestive of dimensional distribution of general cognitive ability, siblings’ mean IQ was slightly lower than controls’, but aforementioned difference did not reach significance.

Possible explanations for the finding of subtle and insignificant differences in terms of emotion recognition performance and general cognitive ability between siblings and control subjects are moderate sample size and self-selection bias. Siblings of patients suffering from schizophrenia are highly aware of psychotic symptoms, thus it is possible that those who find themselves prone to the illness refuse to participate in the study.

4.2. The associations between facial emotion recognition ability and general IQ

Facial emotion recognition ability was significantly associated with general IQ within all three groups of participants (i.e. patients, siblings, controls). Our finding confirmed previous ascertainment that general cognitive ability partially accounts for emotion recognition performance, but that these two cognitive domains are independent from one another (Sergi et al., 2007) since observed correlation coefficients were moderate.

At this stage of analyses both facial emotion recognition and general IQ were analyzed within the same individual. Thus, there was a possibility that one trait was moderated by the other trait or that both traits were secondary to some other unobserved traits of that person. Moreover, since the association between general IQ and DFAR performance in patient group was no longer significant after adjusting for BFRT performance, there was a possibility that general facial recognition ability mediated the aforementioned association in patients. Therefore, we further conducted a cross-trait cross-sibling analysis, in order to rule out the nature of the association between facial emotion recognition ability and general cognitive abilities.
4.3. Facial emotion recognition performance and general IQ cluster within schizophrenia-spectrum families

The within-trait cross-sibling analyses have shown significant familial clustering of both general IQ and facial emotion recognition ability. The covariance of those traits within affected families means that altered facial emotion recognition and general intellectual ability in patient predict alterations in the same cognitive domains in patient’s unaffected sibling. In other words, patients with more disturbances in general cognitive ability and facial emotion recognition ability tend to also have siblings with more pronounced alterations in those cognitive domains in comparison to siblings of cognitively more preserved patients. The observed findings might indicate a possible common etiological influences (i.e. genetic and/or environmental) underlying impaired facial emotion recognition and general cognitive ability in siblings discordant for schizophrenia, since clustering of the aforementioned phenotypes has been observed within the affected families. This could be due to shared genes, shared environment, or due to the influence of epigenetic factors as well, through the gene-environment interaction (The European Network of Schizophrenia Networks for the Study of Gene-Environment Interactions (EU-GEI), 2008). However, future studies should include the control group comprised of healthy pairs of siblings in order to definitely rule out whether the observed associations represent phenomenon specific to schizophrenia, or alternatively, whether they reflect a general effect of siblings having more similar IQ.

4.4. Familial covariation of facial emotion recognition ability and general IQ in schizophrenia

The cross-trait cross-sibling analyses have revealed significant associations between patients’ facial emotion recognition ability and siblings’ general IQ, and between patients’ IQ and their unaffected siblings’ facial emotion recognition as well. This practically means that
patients with worse facial emotion recognition performance tend to have siblings with lower general IQ and that patients with more robust cognitive impairment (i.e. lower IQ) tend to have siblings with more alterations in facial emotion recognition performance. To our best knowledge, this is the first study to date demonstrating significant familial covariation of facial emotion recognition ability and general IQ in siblings discordant for schizophrenia, a finding suggesting a partially shared etiological pathway underlying both features.

Cross-trait cross-sibling approach assures that the association between aforementioned traits exists in an unconfounded fashion (i.e. removes the effects of illness-related factors), since at this stage of analyses facial emotion recognition and general IQ were assessed in different individuals (i.e. patients and their siblings). The presence of such familial covariation was indicative of a common familial (genetic or environmental) etiology of both traits. Since previous research have shown that familial liability to schizophrenia and familial clustering of psychosis-related phenotypes mainly represent the influence of shared genes rather than shared environment (Cardino et al., 2002; Gur et al., 2007; Linney et al., 2003), alterations in facial emotion recognition and general cognitive ability might represent heritable characteristics of schizophrenia. As mentioned earlier, the design of present study does not allow us to conclude with certainty whether the association between general IQ and facial emotion recognition is specific to schizophrenia, or the same familial covariation might also be observed among siblings from the general population.

Some other mechanisms than those abovementioned may also contribute to the observed associations, thus, present findings should be considered in light of their limitations and strengths. This is the first study to demonstrate significant familial covariation of facial emotion recognition and general IQ in siblings discordant for schizophrenia. The advantage of patient-
Sibling based design is automatic control for potential confounding effects associated with the illness (i.e. residual symptoms, medication), and a range of unobserved confounding factors given that those subjects share a lot of socio-economic and developmental conditions. An important issue in sibling-designed studies is a possibility that some of the unaffected siblings use a defensive method of answering, which may cause uncertainty of the obtained data. Nevertheless, we constrained this risk by applying objective/experimental tasks, which represents the strength of our study. Since approximately two thirds of our patients were receiving benzodiazepines, we cannot rule out the possibility that medications influenced their performance on time-dependent WAIS-R subscales and DFAR task. However, when linear regression analyses were performed, benzodiazepine usage did not predict patients' general IQ and overall emotion recognition performance in present research.

Our results are somewhat limited by the fact that the mean age of unaffected siblings was 28.6±6.8 years, thus it is possible that not all of them have passed through a window of risk and some of them (particularly female subjects) could develop schizophrenia beyond the end of the study. Moreover, familial aggregation of traits might be a general phenomenon based on shared genetic and/or environmental factors, thus, the best way to explore cross-sibling associations based upon common schizophrenia predisposition would be to compare findings observed in schizophrenia patients and their siblings with those observed in a healthy group of sibling pairs. Therefore, future studies examining familial covariation of certain phenotypes among siblings discordant for schizophrenia should include control group comprised of healthy pairs of siblings without history of psychotic disorders. Facial emotion recognition alterations might also represent trait markers of the proneness to general psychopathology, since those alterations have also been observed in other psychiatric disorders (Demenescu et al., 2010; Derntl et al., 2009;
Ruocco et al., 2014). Clustering of facial emotion recognition and general intellectual ability is also possible in families that have probands with other psychiatric illnesses, which calls for further research. Apart from that, familial covariation of the examined features in schizophrenia may reflect overlapping neural networks underlying both alterations. The processing of social and non-social information relies on semi-independent networks and neurocognitive and social-cognitive tasks share many cognitive processes, such as working memory and perception. Our results indirectly suggest a possible alteration in those neural networks shared by neurocognition and social cognition, but this assumption requires confirmation by future functional neuroimaging studies.

Alterations in general IQ and facial emotion recognition performance, particularly angry emotion recognition performance, are all associated with liability to schizophrenia spectrum disorders and cluster within families. Thus, all these traits represent important intermediary phenotypes for genetic studies and potential early clinical markers of schizophrenia-spectrum disorders.

**Conflict of interest**

None.

**Role of the Funding Source**

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Acknowledgment

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References


Table 1 Main socio-demographic/clinical characteristics and cognitive performance indices of the sample

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients</th>
<th>Siblings</th>
<th>Controls</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>29.33±5.96</td>
<td>28.56±6.82</td>
<td>29.80±6.34</td>
<td>0.56</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>31 (59.6%)</td>
<td>23 (41.8%)</td>
<td>23 (45.1%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Education (years)</td>
<td>12.48±2.06</td>
<td>13.42±2.58</td>
<td>14.00±2.29</td>
<td>0.00*</td>
</tr>
<tr>
<td>Age at the illness’ onset (years)</td>
<td>24.42±5.10</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Illness’ duration (months)</td>
<td>62.76±56.72</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>52 (100%)</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Mood</td>
<td>16 (30.8%)</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Stabilizers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressants</td>
<td>11 (21.2%)</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>34 (65.4%)</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>IQ</td>
<td>93.42±13.88</td>
<td>105.47±14.33</td>
<td>107.49±17.50</td>
<td>0.00*</td>
</tr>
<tr>
<td>BFRT*</td>
<td>21.40±2.29</td>
<td>22.56±2.18</td>
<td>22.75±2.25</td>
<td>0.01*</td>
</tr>
<tr>
<td>DFAR*</td>
<td>Total</td>
<td>67.26±13.64</td>
<td>76.94±8.41</td>
<td>0.00*</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>69.49±21.21</td>
<td>80.82±17.00</td>
<td>0.00*</td>
</tr>
</tbody>
</table>
### Table 2 Between-group differences on the administered cognitive tests

<table>
<thead>
<tr>
<th></th>
<th>Patients vs Siblings</th>
<th>Patients vs Controls</th>
<th>Siblings vs Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$t/Z^d$</td>
<td>$p$</td>
<td>$t/Z^d$</td>
</tr>
<tr>
<td>WAIS-R$^a$</td>
<td>-4.42</td>
<td>0.00*</td>
<td>-4.53</td>
</tr>
<tr>
<td>BFRT$^b$</td>
<td>-2.35</td>
<td>0.02*</td>
<td>-3.12</td>
</tr>
<tr>
<td>DFAR$^c$</td>
<td>-3.97</td>
<td>0.00*</td>
<td>-4.14</td>
</tr>
<tr>
<td>total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutral</td>
<td>-2.97</td>
<td>0.00*</td>
<td>-2.83</td>
</tr>
<tr>
<td>Happy</td>
<td>-1.90</td>
<td>0.06</td>
<td>-0.19</td>
</tr>
<tr>
<td>Fearful</td>
<td>-3.67</td>
<td>0.00*</td>
<td>-4.14</td>
</tr>
<tr>
<td>Angry</td>
<td>-1.60</td>
<td>0.11</td>
<td>-2.99</td>
</tr>
</tbody>
</table>

*Note:* $^a$WAIS-R$^a$- Wechsler Adult Intelligence Scale- III; $^b$BFRT- The Benton Facial Recognition Task; $^c$DFAR- The Degraded Facial Affect Recognition Task; $^d$Mann-Whitney test (Z) was used to compare skewed measures in between-group comparisons (i.e. BFRT, DFAR), while independent-samples $t$-test was used to assess differences in normally distributed variable IQ (WAIS-R); *p-values ≤ 0.05 were considered significant.
Table 3 Partial correlation analyses: cross-trait within-subject, within-trait cross-sibling and cross-trait cross-sibling associations

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Observed association</th>
<th>$r$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-trait within-subject analysis</td>
<td>$IQ$ patients – $DFAR^a$ patients</td>
<td>0.29</td>
<td>0.03*</td>
</tr>
<tr>
<td></td>
<td>$IQ$ siblings – $DFAR^a$ siblings</td>
<td>0.47</td>
<td>0.00*</td>
</tr>
<tr>
<td></td>
<td>$IQ$ controls – $DFAR^a$ controls</td>
<td>0.33</td>
<td>0.02*</td>
</tr>
<tr>
<td>Within-trait cross-sibling analysis</td>
<td>$IQ$ patients – $IQ$ siblings</td>
<td>0.29</td>
<td>0.04*</td>
</tr>
<tr>
<td></td>
<td>$DFAR^a$ patients – $DFAR^a$ siblings</td>
<td>0.35</td>
<td>0.01*</td>
</tr>
<tr>
<td>Cross-trait cross-sibling analysis</td>
<td>$DFAR^a$ patients – $IQ$ siblings</td>
<td>0.34</td>
<td>0.01*</td>
</tr>
<tr>
<td></td>
<td>$IQ$ patients – $DFAR^a$ siblings</td>
<td>0.29</td>
<td>0.04*</td>
</tr>
</tbody>
</table>

*Note: all analyses were controlled for Age and Sex; *$DFAR$- The Degraded Facial Affect Recognition Task, total score; * $p$-values ≤ 0.05 were considered significant.

Highlights

- Facial emotion recognition and IQ are associated with schizophrenia liability
- Facial emotion recognition and IQ covariate in sib-pairs discordant for schizophrenia
- Siblings had intermediate achievement in angry facial expression recognition
- Objective experimental tasks in sib-pairs study reduce defensive answering risk
- Cross-trait cross-sibling approach assures unconfounded familial clustering analysis