



Impairment of emotional expression recognition in schizophrenia: A Cuban familial association study

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ABSTRACT

It is well established that schizophrenia is associated with difficulties in recognizing facial emotional expressions, but few studies have reported the presence of this deficit among their unaffected relatives. This study attempts to add new evidence of familial association on an emotional expression processing test. The study evaluated the performance of 93 paranoid schizophrenia patients, 110 first-degree relatives of probands from multiplex schizophrenia families, and 109 nonpsychiatric controls on a facial emotional recognition test using a computer morphing technique to present the dynamic expressions. The task entailed the recognition of a set of facial expressions depicting the six basic emotions presented in 21 successive frames of increasing intensity. The findings indicated that schizophrenia patients were consistently impaired for the recognition of the six basic facial expressions. In contrast, their unaffected relatives showed a selective impairment for the recognition of disgust and fearful expressions. Familial association of selective facial emotional expressions processing deficit may further implicate promising new endophenotypes that can advance the understanding of affective deficits in schizophrenia.

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1. Introduction

There is growing body of data indicating that an emotional expression processing (EEP) deficit is associated with cognitive domains in schizophrenia (SZ) (Kohler et al., 2000; Edwards et al., 2002; Sachs et al., 2004; Martin et al., 2005). This deficit is considered a fundamental core disturbance in this illness (Kohler et al., 2004; Gur et al., 2007a). However, there is mixed evidence regarding whether these deficits are specific to SZ (Blair et al., 2004; Pinkham et al., 2007).

EEP have been reported in both first-episode and remitted SZ patients and do not appear to be attributable to the effects of medication, thus this impairment may be state independent (Gur et al., 2007a). In line with these findings, the study of such EEP impairment in non-affected relatives of SZ patients would support the hypothesis of trait status because relatives are not affected by either the confounding variables associated with chronic illness or the medication effects.

First-degree relative's studies suggest that cognitive deficiencies found in the SZ patients' relatives are similar to those found in the patients. These abnormalities are caused by familial predisposition to SZ (Kéri and Janka, 2004; Sitskoorn et al., 2004; Snitz et al., 2006). This

fact led to the familial association concept regarded as the presence of neurocognitive traits in nonaffected relatives of ill probands showing higher deficit rates than the general population (Snitz et al., 2006). Therefore, abnormalities that are overrepresented in unaffected relatives as well as SZ patients are likely to be produced by genes that increase risk of the disorder. This approach has been applied to a number of potential neurobiological SZ markers as a valuable step to explore their utility as endophenotypes (Gottesman and Gould, 2003; Schulze et al., 2003; Schürhoff et al., 2003; Braff et al., 2007). Additionally, the search for cognitive impairments in relatives from multiplex families has proved to be more profitable due to the genetic vulnerability of these families (Tsuang et al., 2006). The strategy of dividing multiplex families (families having at least two SZ patients) from simplex families (families with only one member with SZ) has been useful in detecting the association of higher genetic loading with more severe cognitive deficits, which are potential markers for genetic susceptibility to SZ, in nonpsychotic relatives of SZ patients (Chang et al., 2009).

Few studies have examined the presence of EEP impairment in relatives of people with SZ. Although there are studies that failed to find significant differences on tests of facial affect recognition between relatives and controls (Toomey et al., 1999; Bolte and Poustka, 2003), positive evidence of affect perception deficits were found in unaffected siblings of individuals with SZ (Van't Wout et al., 2007; Leppänen et al., 2008; Alfimova et al., 2009). Gur et al. (2007a) have reported evidence

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of significant impairment in the accurate discrimination of emotion intensity among relatives of multiplex SZ families. Furthermore, Bediou et al. (2007) found an impaired performance of facial emotion recognition in first-episode SZ patients ($n=40$) and their 30 first-degree relatives (30) compared to normal subjects ($n=26$) using sensitive measures of emotional facial expression recognition using morphed faces. These findings suggest that EEP deficit reflects genetic influences shared among SZ families.

However, they highlight the need of further examination of EEP abilities in nonaffected relatives (Gur et al., 2007a).

In line with the prediction that the EEP deficit of SZ patients' relatives is between the controls and patients, the authors' goal was to replicate evidence of familial association of EEP impairment in a large sample of multiplex Cuban SZ families using an emotional expression multimorph task. The existence of familial association for the emotion recognition deficit in Cuban SZ families could support this cognitive impairment as an endophenotypic marker useful for genetic analyses of these complex psychiatric disorders in this population.

2. Methods

2.1. Participants

A total of 312 subjects were studied; of these, 93 were paranoid schizophrenic patients, 110 unaffected first-degree relatives, and 109 normal subjects.

The patients were all diagnosed with paranoid SZ and recruited through the Havana Centers of Mental Health. The group of SZ patients included 63 males and 31 females aged 20–58 years with a median of 34.8 years. In this study, we did not report the years of education. Instead, we analyzed the different groups taking into account the three educational levels existing in our country: 22 patients (23.6%) had secondary educational level, 53 (56.9%) pre-university, and 13 (13.9%) university level.

They were selected from multiplex SZ families based on the presence of two or more SZ-affected subjects in the studied families. Diagnoses were confirmed by experienced psychiatrists by means of the Spanish version of the Schedules for Clinical Assessment in Neuropsychiatry (Vázquez-Barquero, 1982). The Present State Examination (PSE)-10 was carried out on all studied patients. This semi-structured clinical interview is based on Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria (American Psychiatric Association, 1994).

Symptom severity was assessed with the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). Mean ratings were 18.08 (± 10.01) on the positive symptom scale and 20.90 (± 11.05) on the negative symptom scale. Patients, during remission of symptoms, were receiving maintenance antipsychotic medicine: 85 (90%) on typical antipsychotics, 5 (5.3%) on atypical antipsychotics, and four (4.7%) patients receiving both types of antipsychotics.

The group of relatives were recruited through the probands of this study. A total of 110 healthy first-degree relatives were included (65 males and 45 females). The age of the relatives ranged from 20 to 58 years with a median of 42.01 years. Twenty-six relatives (23.6%) had secondary educational level, 51 (46.3%) pre-university, and 30 (27.2%) university level.

A maximum of four first-degree relatives was recruited per family. Familial psychiatric morbidity was investigated using the Family Interview for Genetic Studies, FIGS (Maxwell, 1992). A complete family history of first-degree relatives was obtained from each probands and from at least one first-degree relative and it was conducted by psychiatrists formally trained to use the FIGS instrument. None was taking psychopharmacological medication. The information was supplemented, if required, with data from the medical case notes.

Control subjects were recruited through local recruitment efforts. This group comprised 109 unrelated subjects (40 males and 69 females) aged 20–58 years with a median of 33.6 years. Nine controls (8.26%) had a secondary educational level, 53 (48.6%) pre-university, and 47 (43.12%) university level.

The exclusion criteria for relatives and controls subjects were: i) absence of past or present neurological or psychiatric illnesses, ii) history of traumatic brain injury or body-motor impairments, and iii) history of substance abuse, addictions, or use of neuroleptics. All subjects reported normal or corrected-to normal vision.

Written informed consent was obtained from all participants after complete description of the study. The study was performed in accord with the World Medical Association (Declaration of Helsinki) ethics code and the institutional ethics committee.

2.2. Emotional expression multimorph task (EEMT)

The task is a variation of the paradigm described by Blair et al. (2004). This is a dynamic test that requires recognizing six different basic facial emotional expressions (happiness, surprise, fear, sadness, disgust, and anger). In the current version of this paradigm, the presentation of 48 transformation sequence trials (six emotions \times eight models) in random order was presented.

Each trial was composed of 21 morphed images which changed from a neutral face (0% expression) through 21 stages in 5% increments into one of six prototypical emotional expressions (100% expression). The facial images were displayed in the center of the screen with a 200 ms stimulus transformation rate. Before the task, participants saw a word list of the six basic emotions and were instructed to detect, in each trial, the emotional expression as soon as they recognized it. During the EEMT, the pictures morphed until participants got the correct responses. A trained interviewer pressed a button when the subjects thought they recognized the emotion to avoid biases in pattern of responding.

When subjects made a correct response the trial finishes, otherwise the trial continues.

The EEMT measures sensitivity and accuracy of individuals to detect each facial emotional expression. Sensitivity was defined as the average number of stages viewed before correct recognition (based on correct responses). Accuracy was calculated as the proportion of correct recognitions for each emotional expression considering the participants' final responses.

2.3. Data analysis

We compared demographic characteristics between groups using chi-squared tests for categorical variables and analysis of variance (ANOVA) for continuous variables. Concerning the years of education variable, comparison among the three groups was best conducted by the Kruskal–Wallis H -test.

Performance, i.e., sensitivity and accuracy on the EEMT, is analyzed with a multivariate analysis of covariance (MANCOVA), which was used to test the hypothesis that the three groups (SZ patients, first-degree relatives, and normal subjects) differed significantly with respect to the mean recognition stage scores (sensitivity) and mean error scores (accuracy) for each of the expressions. Age, gender, and educational level were considered as covariates in our model.

When significant multivariate effects were found, multivariate tests for planned contrast analyses comparison among groups were conducted with an accepted significance level of $P < 0.05$. To explore the extent to which emotional expressions in EEMT performance have a familial component, Pearson's correlations of performance scores between SZ patient and their first-degree relatives were calculated.

3. Results

3.1. Group demographic comparisons.

The three groups differed significantly in terms of educational level ($\chi^2 = 20.96$, $df = 2$, $P < 0.001$). Multiple comparison analysis indicated that the control group had a higher educational level than the relatives group ($P = 0.003$) and the group of patients ($P < 0.000$) who did not differ from each other ($P = 0.339$). The three groups differed in age ($F(2, 307) = 21.58$, $P < 0.001$), being the relatives older than both the patients ($P < 0.001$) and the controls ($P < 0.001$) who have similar ages ($P = 0.693$). The three groups also differed in gender ($\chi^2 = 22.29$, $df = 2$, $P < 0.001$). The patient group included more males than relatives ($P = 0.002$) and control groups ($P < 0.001$).

Therefore, in order to show that the significant differences among groups were not attributable to group differences in age, gender, and educational level; MANCOVAs were computed with those variables as covariates.

3.2. Comparison of emotional expression multimorph task performance (EEMT) between groups

3.2.1. Sensitivity for different emotions

Fig. 1 shows the average of EEMT sensitivity between SZ patients, their relatives, and controls. As can be seen, the healthy controls showed the lowest threshold levels (higher sensitivity) of correct recognition of emotional stimuli regardless of emotional expressions, where the happy was the easiest emotion to recognize.

Table 1 shows the EEMT performance by subject group. A 3×6 MANCOVA was conducted with group (SZ patients, first-degree relatives, and controls) as the between-factors and mean expression recognition scores as dependent variables (happy, surprised, disgusted, angry, sadness, and fearful).

The results of the MANCOVA revealed a main effect of group (Wilks's test = 0.890, $F = 2.75$, $df = 12$, $P = 0.001$), age (Wilks's test = 0.936, $F = 2.75$, $df = 6$, $P = 0.005$), and educational level (Wilks's test = 0.916, $F = 2.07$, $df = 12$, $P = 0.017$). There was no main effect of sex nor any

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