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Depressive symptoms evaluated by the Calgary Depression Scale for Schizophrenia (CDSS): Genetic vulnerability and sex effects

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ABSTRACT

The present study compares the occurrence of depressive symptoms evaluated by the Calgary Depression Scale for Schizophrenia (CDSS) in patients of Multiplex (MS) and Simplex Schizophrenia families (SS). The Positive and Negative Syndrome Scale (PANSS) was used to evaluate psychopathology. A total of 206 paranoid schizophrenia patients were studied according DSM-IV criteria. The Family Interview for Genetic Studies (FIGS) was used to study the families. A result in the FIGS for a positive family history of schizophrenia was referred as MS (patients); its lack as SS (patients). CDSS scores were compared among MS and SS patients and possible sex differences intra- and inter-groups were explored. In the analysis of our sample (30) 19% of the total persons with schizophrenia group was depressed. The depressive symptoms measured by the CDSS were higher in females and the MS males group. Males from MS group showed more depressive symptoms than males from SS group. No differences with females from both groups were found. Findings in this study underscore the importance of gender and family history in understanding the heterogeneity of schizophrenia. This study suggests that sex and familiar history are important to consider in studying depressive symptoms.

1. Introduction

Depression is a frequent symptom in schizophrenia. This observation was originally made by Bleuler, who considered anhedonia and disorders of affect to be important aspects of schizophrenia, and depression has continued to be recorded as definitions of schizophrenia have changed and evolved (Siris, 1991). The reported rate of depression is 7 to 75%, with a modal rate of 25% (Möller, 2005; Rocca et al., 2005; Maggini and Raballo, 2006). Depression symptoms are indeed frequent in schizophrenia in all the illness phases (Zisook et al., 2006). Differences in cohort status, illness chronicity and assessment methods contribute to the variability of these estimates (Rocca et al., 2005).

There are contradictory findings on the origins of depressive symptoms in schizophrenia. There are several theories that posit depressive symptoms as having a multifactorial etiology: they may be a part of the pathology or they may be reactive post-psychotic, pharmacogenic or akinetic (Bressan et al., 2003).

Some research support the hypothesis that depressive symptoms are an integral part of schizophrenia (Bressan et al., 2003). Depressive symptoms in schizophrenia spectrum disorders are not an epiphenomenon. Factor-analytic studies of symptoms in large samples of patients consider depressive symptoms as one of the psychopathological domains of schizophrenia in addition to positive, negative, excitement and cognitive domains (Cuesta and Peralta, 2001).

Depressive symptoms have been associated to several negative aspects of the clinical outcome, including cognitive impairment, deterioration of psychosocial functioning, increased relapse risk, longer hospitalization periods, poorer response to medication, chronicity and increased suicide risk (Bressan et al., 2003). However, the two most frequently used diagnostic classifications in psychiatry, DSM-IV and ICD-10, differ in their approach to depressive symptoms in schizophrenia. DSM-IV (American Psychiatric Association, 1994) does not identify depressive episodes in the majority of clinically stable schizophrenia patients (Bressan et al., 2003). ICD-10 has a specific diagnostic criterion for depression in schizophrenia called post-

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schizophrenic depression. On the other hand, DSM-IV does not have any category in the main classification (Bressan et al., 2003). This has research and clinical implications. In the clinic side, faithful adherence to the present classification system could lead to misdiagnosis and under-treatment of depressive episodes in schizophrenia.

Depression occurring in schizophrenia is a common problem; however, investigators have typically not studied it with the paranoid/nonparanoid dichotomy in mind. The reports of depression for different types of schizophrenia have been contradictory. For example, it has been found that patients with a paranoid type of schizophrenia were the least depressed and had the fewest fluctuations of mood (Strian et al., 1981). But a very different idea was presented in another study: depressed mood and anhedonia constitute serious problems for schizophrenia patients, particularly for paranoid schizophrenia patients during the postpsychotic phase of their illnesses (Candido and Romney, 2002).

The 1933 introduction of schizoaffective disorder recognized the diagnostic relevance of mood symptoms in psychotic patients, linked schizophrenia (psychosis) and mood disorders, and eroded the concept of the Kraepelinian dichotomy. Some authors now consider schizoaffective disorder to be a psychotic mood disorder and not a subtype of schizophrenia or a separate disorder. In addition, certain investigators have associated paranoia with depression and delusional guilt (Lake, 2008).

Comparative clinical and recent molecular genetic data find phenotypic and genotypic commonalities between patients diagnosed with schizophrenia and psychotic bipolar disorder supporting the idea that paranoid schizophrenia could be the same disorder as psychotic bipolar disorder (Lake, 2008). On the other hand, a recent study found cognitive and emotion-related processes to be involved in paranoid delusions (Bentall et al., 2009).

The Calgary Depression Scale for Schizophrenia (CDSS) has emerged as a valid instrument for assessing depressive symptoms in schizophrenia (Addington et al., 1993). This scale enables depression to be assessed independently of negative or extrapyramidal symptom-related depressive phenomena in schizophrenia (Addington et al., 1994). Psychometric properties of the CDSS have been widely documented in stabilized patients (Collins et al., 1996; Kontaxakis et al., 2000; Lançon et al., 2001; Kim et al., 2006).

In schizophrenia, not all clinical dimensions related to genetic vulnerability are equally reported. For example, in the case of negative symptoms, they are probably more heritable and may have stronger genetic bases than positive symptoms (Dworkin and Lenzenweger, 1984; Martin et al., 2004).

There are projects examining the relationship between depressive symptoms measured by CDSS versus those assessed with the Positive and Negative Syndrome Scale (PANSS) (Collins et al., 1996; Kim et al., 2006). The depression scale was found to be highly correlated with the negative symptoms subscale (Kontaxakis et al., 2000; Rocca et al., 2005). However, other studies reported correlation with positive, negative and general psychopathology (Lançon et al., 2001).

Many studies support the presence of significant differences between males and females with schizophrenia arising from the interplay of sex hormones, neurodevelopmental and psychosocial sex differences (Leung and Chue, 2000). Sex differences in schizophrenia have been associated with the onset year and the course in cognitive and neuropsychological functioning (Bozikas et al., 2006; Weiss et al., 2007). Studies on affective disorders without psychotic features report a sex ratio for depression in females – males equal to 1.5–3:1 (Angst et al., 2002; Marcus et al., 2005). With these numbers, it is possible that partly different biological mechanisms in females and males with schizophrenia are involved, and they could also lead to different depression phenomena.

Schizophrenia is a complex, multifactorial and polygenic disease (Thibaut, 2006). Therefore, the distribution of impairment among schizophrenia families is consistent with multifactorial models of familial transmission. Presumably, families with more than one affected or Multiplex Schizophrenia (MS) families have more genetic susceptibility to the illness than families with just one affected or Simplex Schizophrenia (SS) families, putting relatives at greater risk for MS families (Seidman et al., 2003). It is hypothesized that the higher the number of affected members in a family (MS), the more likely they are to have a genetic vulnerability to the illness, while those patients belonging to the group with a negative family history are considered to have a more environmental form and less genetic vulnerability (Tsuang et al., 2006).

Peralta and Cuesta (2007) reported in a familial liability study that categories of psychotic disorders are on a continuum of familial liability to schizophrenia and mood disorder. “More specifically, a relatively broad phenotype including either early age at onset or lack of affective features appears to be closer to familial liability than the highly restrictive phenotypes such as DSM-IV and Kraepelinian diagnostic concepts” (Peralta and Cuesta, 2007).

That is why the purpose of this study is to research the pattern of occurrence and features associated with depressive symptoms evaluated by the Calgary Depression Scale for Schizophrenia (CDSS) in schizophrenia patients from MS and SS families and its relation with the sex factor.

2. Methods

2.1. Subjects

A total of 206 paranoid schizophrenia outpatients in the stable period were recruited from 3 community mental health centers in Havana City. Patients were selected only from families who agreed to participate. A written informed consent was obtained from the families. Only 31.6% outpatients or families from community mental health centers refused to participate and 9.1% left the study.

Diagnoses were confirmed using the Spanish version of the semi-structured clinical interview, the Present State Examination (PSE-10) derived from the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) created by the World Health Organization (WHO) (Vázquez-Barquero, 1992). This study is part of a family study to search for endophenotypes in schizophrenia organized by Cuban Neuroscience Center. Schizophrenia was considered stabilized if patients had their antipsychotic regimen unchanged for the last 6 months and were judged clinically stable by the specialists from community mental health centers. Excluded from the study were patients with alcoholism, substance abuse, and other organic causes of depression.

The interviewers were psychiatric specialists previously trained by the WHO in the SCAN system. The convergence in the classification by the two measures was calculated by Kappa (κ). Inter-rater reliability was high for the overall diagnostic (kappa coefficient = 0.70) (Martin et al., 1997). The diagnostic criteria applied were those of the DSM-IV (American Psychiatric Association, 1994). All the patients accepted and signed the terms of the informed consent to participate in the study. The research reported in this article was reviewed and approved by the Cuban Neuroscience Center Research Board and is in compliance with the ethical rules for human experimentation as stated in the Declaration of Helsinki.

2.2. Clinical assessments

Depressive symptoms were evaluated using the Spanish version of the CDSS (Sarro et al., 2004). The CDSS is an observer-rated scale, based on semi-structured, goal-directed interviews, specifically developed for the assessment of the level of depression in schizophrenia. The presence or absence of clinically significant depression was determined using a cut-off point ≥ 6 (Addington et al., 1992).

The Spanish version of the PANSS (Kay, 1987) was used to evaluate positive and negative symptoms and general psychopathology. The interviewers were psychiatric specialists previously trained in the use of the scales.

2.3. Family study

The Family Interview for Genetic Studies (FIGS) (NIMH-Molecular Genetics Initiative, Maxwell 1992) was used for the family study. The FIGS is a guideline used to gather diagnostic information on the relatives of patients with schizophrenia and bipolar disorders. A genealogical tree was constructed before applying this instrument and it was reviewed with the participants. For each subject, at least two non-affected key informant first degree relatives were interviewed by a psychiatric specialist trained to use the instrument (without knowledge of the CDSS results). In this study we used the Spanish version validated in our country (Diaz de Villalvilla et al., 2008).

None of the informants were diagnosed with schizophrenia related disorders according to the FIGS interview. Family history information was complemented by