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A proton magnetic resonance spectroscopy study in schizoaffective disorder: Comparison of bipolar disorder and schziophrenia

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ABSTRACT

The aim of this study was to compare schizoaffective disorder, bipolar disorder and schizophrenia based on ^{1}H-MRS metabolite values in dorsolateral prefrontal cortex and executive functions. The subjects comprised 15 patients with bipolar disorder type I (BD), 15 with schizophrenia (SCH), 15 with schizoaffective disorder (SAD) and 15 healthy controls. We performed proton magnetic resonance spectroscopy (^{1}H-MRS) of the dorsolateral prefrontal cortex (DLPFC) bilaterally. Levels of N-acetyl aspartate (NAA), choline-containing compounds (Cho) and creatine-containing compounds (Cr) were measured in the DLPFC using ^{1}H-MRS. We administered the Wisconsin Card Sorting Test (WCST) and the Stroop Test (ST) to evaluate executive functions. The SAD, BD and SCH patients had lower levels of NAA than the control group. The SAD and BD patients had low levels of Cho compared to the control group. The left DLPFC Cr levels in all of the patient groups and the right DLPFC Cr levels in the BD and SAD groups were lower than in the control group. The levels of NAA Cho and Cr were not related to executive functions and attention performance. Cr level were related to attention processes, only in SCH. Our results indicate that NAA levels are reduced in schizoaffective disorder, bipolar disorder and schizophrenia, but the reduction in the levels of NAA is not a distinctive feature among these three illnesses. Schizoaffective and bipolar disorders have similar features related to the levels of compounds containing Cho and Cr. This similarity may be related to these illnesses both having an affective basis.

1. Introduction

The term schizoaffective disorder refers to the coexistence of schizophrenia and affective symptoms. This illness involves diagnostic ambiguities because of its intrinsic complexity, its heterogeneity and the lack of clear boundaries between schizophrenia and mood disorder (Kendler et al., 1995). According to the Diagnostic and Statistical Manual of Mental Disorders-IV, Revised (DSM-IV-R), the diagnosis of schizoaffective disorder requires that an affective disorder and psychotic symptoms be observed together, and the psychotic symptoms must exist for at least two weeks when there are no affective symptoms. Bipolar and depressive types of schizoaffective disorder are defined. Psychotic symptoms, such as delusions and hallucinations, can accompany depression symptoms in schizodepressive type, and mania symptoms can accompany schizomanic type. Occasionally, affective symptoms can be so strong and psychotic symptoms so weak that it can be difficult to distinguish the illness from a mood disorder (APA, 1994). Schizoaffective disorder was included in affective disorders in International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) draft in April 1987, it was included in psychotic disorders in ICD-10 draft in April 1988. Diagnosis of schizoaffective disorder is depends upon an approximate "balance" between the number, severity and duration of the schizophrenic and affective symptoms according to ICD-10 (Ceylan, 2002).

Cardno et al. (2012) have suggested that inter-rater reliability are lower in schizoaffective disorder than those of schizophrenia and bipolar disorder. It was reported that rate of co-occurrence in schizoaffective mania and mania are great within twin probands and twin pairs. The authors of a review study that examined to family, twin, and adoption studies reported that schizoaffective disorder probably phenotypical variations or expressions of genetic interforms between schizophrenia and affective disorder (Bertelsen and Gottesman, 1995). Kendler et al. (1995). reported that relatives of probands with schizoaffective disorder had significantly higher rates of affective illness than relatives of schizophrenia probands and significantly higher rates of schizophrenia than relatives of probands with affective illness.

Abbreviations: H-MRS, proton magnetic resonance spectroscopy; BD, bipolar disorder; SAD, schizoaffective disorder; SCH, schizophrenia; DLPFC, dorsolateral prefrontal cortex; NAA, N-acetyl aspartate; Cho, choline-containing compounds; Cr, creatine-containing compounds; WCST, Wisconsin Card Sorting Test; ST, Stroop Test.

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The relationship among schizoaffective disorder, schizophrenia and mood disorders is defined by six possibilities. Schizoaffective disorder is examined as potentially being an atypical schizophrenia with affective symptoms, an atypical mood disorder with psychotic symptoms, a co-diagnosis of schizophrenia and mood disorder, an illness that is independent of schizophrenia and mood disorder, or a complex illness that is composed of schizophrenia and mood disorder. However, some authors suggest that there is only one psychosis and that schizophrenia and mood disorders constitute the endpoints of a spectrum, with schizoaffective disorder lying in the middle of the spectrum. According to the current classification systems, a patient can be diagnosed with schizoaffective disorder if he/she has one of the above six clinical presentations (Forrester et al., 2001; Peralta and Cuesta, 2008). In a review of the literature, Cheniaux et al. (2008) concluded that schizoaffective disorder is a heterogeneous illness consisting of schizophrenia and mood disorder and that it exists on a spectrum between schizophrenia and mood disorder.

The clinical presentation of schizoaffective disorder is difficult to distinguish from bipolar disorder and schizophrenia. Comparing the effects of these chronic illnesses on cognitive functions may contribute to understanding of how they are related. Studies have found that there is deterioration in attention, memory and executive functions in the euthymic period of bipolar disorder and that residual symptom negatively affect cognitive functions (Chaves et al., 2011; Elshahawi et al., 2011; Malhi et al., 2007). In patients with schizophrenia, studies have found deterioration in many cognitive functions, such as attention, executive function, working memory, verbal and visual memory, learning and processing speed (Béchard-Evans et al., 2010; Mahurin et al., 1998; Perlstein et al., 2001). Patients with schizoaffective disorder have shown more deterioration in the cognitive domains, such as attention, executive functions and verbal memory, than healthy controls and bipolar patients with psychotic features; related to these problems, patients with schizoaffective disorder also experience more difficulties at work (Bowie and Harvey, 2005; Torrent et al., 2007). Some authors have suggested that patients with schizoaffective disorder are not different from patients with schizophrenia with regard to basic cognitive functions, including social cognitive functions, executive functions, memory and processing speed (Fiszdon et al., 2007). The authors of a comparative study determined that patients with schizophrenia had the most deterioration in executive functions, followed by those with schizoaffective disorder and then those with bipolar disorder with psychotic features (Szoke et al., 2008).

Proton magnetic resonance spectroscopy (^{1}H-MRS) is an imaging technique that can noninvasively measure the biochemical structures and the metabolites of tissues and present them in one spectrum. In the evaluated region, the levels of neurochemical compounds containing N-acetyl aspartate (NAA), creatine (Cre), choline (Cho) and compounds such as myo-inositol (Myo-I) can be determined in vivo (Yildiz-Yesiloglu and Ankerst, 2006). In bipolar disorder, authors have reported a decrease in the levels of dorsolateral prefrontal cortex (DLPFC) NAA and a relationship between the number of past affective episodes and the levels of Cho-containing compounds (Sassi et al., 2005); levels of NAA are low in children who have at least one parent with bipolar disorder, and low NAA can be a marker for bipolar disorder (Chang et al., 2003). On the contrary, some studies indicate that there is no difference in the levels of DLPFC molecules containing NAA, Cho and Cr in bipolar disorder groups and control groups (Brambilla et al., 2005; Scherk et al., 2009). In studies of patients with schizophrenia, decreases in the ratios of DLPFC NAA/Cre and NAA/Cho have been found (Bertolino et al., 1996); NAA/Cr levels are lower in patients with a deficit syndrome than in control groups and patients with schizophrenia who do not have apparent deficits (Delamillieure et al., 2000). The number of studies reporting that there is a relationship between the levels of frontal lobe NAA and cognitive functions, especially in schizophrenia, is progressively increasing (Bertolino et al., 2000; Galińska et al., 2007; Ohrmann et al., 2009).

Schizoaffective disorder has not yet been analyzed sufficiently in terms of executive functions and DLPFC neurochemical changes. Data suggest that patients with bipolar disorder, schizoaffective disorder and schizophrenia will experience changes in levels of DLPFC NAA, compounds containing Cho and compounds containing Cr; these data also suggest that schizoaffective disorder will be detected similarly in terms of executive function and DLPFC neurochemical metabolites among patients with schizophrenia. This study determined the executive functions and DLPFC neurochemical metabolite levels in patients with bipolar disorder, schizoaffective disorder and schizophrenia and compared patients with schizoaffective disorder with patients with bipolar disorder and schizophrenia.

2. Materials and methods

2.1. Study design

Fifteen healthy controls, 15 patients diagnosed with schizoaffective disorder (SAD), 15 patients with bipolar disorder type I (BD) and 15 patients with schizophrenia (SCH), according to the DSM-IV diagnostic criteria, were included in the study. The patients had been followed by the Mood Disorder and Psychosis clinic in the Department of Psychiatry at the Pamukkale University School of Medicine. The inclusion criteria were that individuals be between the ages of 18 and 60, be literate at a level sufficient for reading and not have had a mood or psychotic episode in the last three months. The exclusion criteria were mental retardation, alcohol or substance abuse before the study that could affect the symptom distribution, electroconvulsive therapy in the prior six months and neurological and organic mental disorders. The control group was composed of healthy individuals whose age and gender was similar to the patient groups and who had no physical or mental disorders. Ethics committee approval was obtained from the local ethics committee of Pamukkale University in accordance with the Declaration of Helsinki. Patients were informed about the study, and only those who gave written consent were included.

Psychiatric diagnoses were made using Structured Clinical Interviews for the DSM-IV (SCID- I) (Özkürkçügil et al., 1999). A questionnaire collecting sociodemographic data and information about clinical features of the illness for the individuals included in the study was completed by the researchers. Patients with mood episodes or psychotic relapses in the prior three months were excluded from the study. For patients with BD and SCH, the Hamilton Rating Scale for Depression (HAM-D) (Akdemir et al., 2001; Hamilton, 1960) and the Young Mania Rating Scale (YMRS) (Karadag et al., 2001; Young et al., 1978) were applied. To determine the presence of psychotic symptoms, the Positive and Negative Syndrome Scale (PANSS) (Andreasen, 1990; Erkoç et al., 1991a,b) and the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962) were applied to the SAD and SCH patients. A bilateral proton magnetic resonance spectroscopy (^{1}H-MRS) of the DLPFC region was conducted for the patients and the control group. Neuropsychological tests were administered by a psychologist trained in this subject.

2.2. Neuropsychological evaluation

Executive functions were evaluated using the Wisconsin Card Sorting Test (WCST) and the Stroop Test (ST). The WCST was developed by Heaton (Heaton et al., 1993) and relies on the matching principle. Performance in the WCST involves generating the matching rule based on positive feedback, being able to pay selective attention to the card features and feedback from the test administrator, using the matching principle as long as it is in effect and abandoning the