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Executive deficits: A continuum schizophrenia–bipolar disorder or specific to schizophrenia?

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ABSTRACT

Executive dysfunction is a core deficit in schizophrenia (SCH). However, some controversy exists when examining such deficits in studies of bipolar disorder (BD). The aim of the present research was to investigate whether executive deficits were similar or distinct in both illnesses. 148 patients with BD, 262 patients with stable SCH and 108 healthy controls (CT) were recruited for the study. The BD patients were also differentiated according to the clinical subtype (BD subtype I, BDI, or subtype II, BDII) they exhibited and according to whether there was a previous history of psychosis. All subjects completed a broad neuropsychological battery. The influences of other clinical data were also evaluated. Both the BD and SCH patients showed widespread deficits in all executive tasks, with no differences between these two groups of patients. BDII patients only showed some selective deficits, and their scores on planning and inhibitory tasks fell on the continuum between the CT, the BDI and the SCH patients. Psychotic phenotypes did not influence the BD patients' performance on the battery. Other clinical variables related to illness severity did influence deficits in any subgroup of patients. Our results point to the existence of common executive disturbances in both diagnostic categories. Moreover, the inclusion of subclinical phenotypes in research may be helpful in cognitive assessment studies.

1. Introduction

A growing body of evidence suggests that schizophrenia (SCH) and bipolar disorder (BD) share some common genetic vulnerabilities, which may manifest as overlapping neuropsychological impairments (Glahn et al., 2006). The inability to plan or execute tasks may exacerbate the course of illness in these patients because it may adversely influence social performance, functional outcome, quality of life or treatment adherence (Altshuler et al., 2008; Tolman and Kurtz, 2012). Several studies have implicated executive functioning as one of the most promising endophenotypes of psychiatric disorders (Savitz et al., 2005; Robinson et al., 2006; Taylor, 2007). In fact, impairments in executive functioning are considered a primary deficit in schizophrenia. However, studies analyzing the performance of euthymic bipolar subjects have yielded conflicting results (Cavanagh et al., 2002; Mur et al., 2007; Thompson et al., 2009; Bora et al., 2009; Lee et al., 2013): although some studies have found disturbances in executive functioning to be similar between BD and SCH patients (Martinez-Aran et al., 2002; Verdoux and Liraud, 2000; Pradhan et al., 2008), others argue that BD patients perform at a level between SCH and healthy subjects (Rossi et al., 2000; Altshuler et al., 2004; Trivedi et al., 2007; Krabbendam et al., 2005) or even that BD patients perform within normal limits on several of these tasks (Cavanagh et al., 2002; Zalla et al., 2004; Wobrock et al., 2009). One of the possible causes of these conflicting results is that the different clinical phenotypes (e.g., BD subtypes I/II, patients with other comorbidities such as psychotic episodes or alcohol/drug abuse, first-episode or chronic patients, remitted or acute patients) might be related to different deficits in cognitive functioning. Consequently, the extant literature has emphasized the need for larger samples so that differentiation into specific subgroups with similar cognitive deficits can be attempted (Martinez-Aran et al., 2002). For example, nearly all BD research has focused on BD as a diagnostic

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category or solely on BD subtype I; this focus is mainly attributable to the small number of patients with BDII who could be recruited (Torrent et al., 2006). Although the literature presents the picture that more severe cognitive dysfunction accompanies BDI compared with BDII (Simonsen et al., 2008; Li et al., 2012), recent research supports the idea that some neuropsychological disturbances are evident in the latter group (Torrent et al., 2006; Hsiao et al., 2009) and even suggests that some cognitive dysfunctions may be quantitatively more marked in this subgroup (Summers et al., 2006; Harkavy-Friedman et al., 2006). For another example, a previous history of psychosis has been regarded as a clinical marker of a more severe course of illness in BD, and consistent with these findings, some authors measured greater cognitive disturbances in this subset of patients (Levy and Weiss, 2010). Nevertheless, the existence of controversial results in the literature (Brissos et al., 2011) indicates the need for replication studies. One other possible cause of the different outcomes on executive functioning measures between patients with SCH and BD may be the tendency to include patients who are unstable during the study, possibly experiencing manic, depressive or acute psychotic episodes (Martinez-Aran et al., 2002; Ryan et al., 2012). In contrast, studies of stable patients may help in the identification of trait deficits that persist during remission periods.

Due to the existence of these previous conflicting results, the diagnostic specificity of executive deficits needs further clarification. The aim of the current study is to investigate executive functioning in stable SCH and euthymic BD patients using several measures of this cognitive domain. As a second objective, we examine these deficits in different classifications of BD. Finally, we analyze these disturbances in executive performance for evidence that they may be influenced by the clinical progression of the illnesses.

2. Material and methods

2.1. Subjects

Subjects were recruited from the Mental Health Area of the Hospital Clínico San Carlos (Madrid, Spain) and the Hospital Virgen de la Luz (Cuenca, Spain). A total of 518 individuals, aged 18–65 years, were enrolled for the study: 148 were diagnosed with BD, 262 were diagnosed with SCH and 108 were healthy control subjects. Diagnoses were made according to DSM-IV criteria. The patients were evaluated with the Structured Clinical Interview for DSM-IV (SCID-I:P) and the control subjects were screened using the SCID-I non-patient version to exclude subjects with prior psychiatric histories. The BD patients were euthymic according to the Van Gorp criteria (van Gorp et al., 1998): scores <7 on the Hamilton Depression Rating Scale (HDRS) and <6 on the Young Mania Rating scale (YMRS) were maintained for at least three consecutive monthly assessments. SCH patients were regarded as stable if the total PANSS-P score change was <3 points and there were no pharmacological changes for at least three months prior to administration of the neurophysiological tests.

Exclusion criteria included the following: severe medical or neurological disease (e.g. cancer, diabetes, HIV, multiple sclerosis); illiteracy or low education levels that hindered cognitive assessment; mental retardation; a history of electroconvulsive therapy (ECT) in the last two years; substance dependence or abuse (except for tobacco consumption) at the time of the study; and head injury with loss of consciousness. When recruitment of patients started, a total of 111 patients (73 SCH, 38 BD) were not considered for the study according to the exclusion criteria. Specific reasons for the exclusion were: drug/alcohol abuse (63 SCH, 31 BD), low cognitive levels (7 SCH, 6 BD) and severe medical disease (3 SCH, 1 BD). After their inclusion in the study, 14 patients (9 SCH, 5 BD) dropped out of the study. Control subjects had no first-degree relatives with bipolar disorder, schizophrenia or other psychiatric disorders. Additional demographic and clinical information was collected on all participants using a semi-structured questionnaire. The investigation was carried out according to the Declaration of Helsinki. All subjects provided informed consent in writing and ethical approval for the study was obtained from both hospitals.

2.2. Neuropsychological measures

All study subjects received a broad executive neuropsychological assessment. The vocabulary subtest of the Wechsler Adult Intelligence Scale (WAIS) was used to estimate premorbid IQ (Lezak, 1995). The test battery that assessed the distinct dimensions of executive functioning included the Wisconsin Card Sorting Test (WCST) (Berg, 1948), the Trail Making Test (TMT) Parts A and B (Reitan, 1958), the Digit Span subtest of the Wechsler Adult Intelligence Scale—Revised (Wechsler, 1981), the phonological (FAS) and semantic (Animals) verbal fluency tests (Benton and Hamsher, 1989), the Stroop Color-Word Interference Test (SCWT) (Stroop, 1935) and the Tower of Hanoi puzzle (TOH) (Borys et al., 1982).

2.3. Statistical analysis

Statistical analyses were performed using SPSS 16.0 for Windows (Chicago, IL, USA). Demographic and clinical analyses were performed with χ^2 tests (for qualitative variables) or with ANOVA (for quantitative variables). Neurocognitive variable distributions were assessed for normality, and when necessary, appropriate logarithmic and inverse transformations were made. The scores on the executive tests were then standardized relative to the performance of the control group (*Z*-scores: the mean of control population − raw value divided by the standard deviation of the control group) to facilitate comparisons across the tests. In addition to the individual measures, a *Z*-score composite was calculated by summing the *Z*-scores for each test. ANOVA was performed to compare scores between the groups. Post-hoc pairwise comparisons were accomplished via the Bonferroni procedure. An ANCOVA was used to control for sociodemographic variables (viz., age, gender, years of education and IQ). Group (BD, schizophrenia or controls) was selected as the between-participants factor and *Z*-scores were entered as dependent variables. Other diagnostic subdivisions (viz., BD I subtype, $N = 118$, vs. BDII subtype, $N = 30$; presence, $N = 93$, vs. absence of previous psychotic history, $N = 55$) were also analyzed. Effect size (Cohen's *d*) was computed using the following formula: $d = M_1 - M_2/S_{pooled}$ (Cohen, 1988). Significance levels were set at p-value ≤ 0.05.

3. Results

3.1. Sociodemographic and clinical data

Table 1 shows the demographic and clinical features and the comparisons between groups. In the BD group, 118 subjects (79.7%) were diagnosed with BD subtype I (BDI). In this group, 93 patients (62.8%) had histories of previous psychotic episodes. Other demographic and clinical features and comparisons between groups are presented in this table.

3.2. Neurocognitive assessment

Table 2 and Fig. 1a summarize how the groups performed in all of the executive function tasks. The means and standard deviations are provided for the raw scores, prior to transforming for normality or calculating *Z*-scores. The patients performed worse than the