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Neuropsychological correlates of symptom dimensions in inpatients with major depressive disorder

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ABSTRACT

Symptoms of major depressive disorder (MDD) manifest variably across individuals. Accordingly, recent models of the disorder imply that MDD may be characterized according to independent symptom dimensions. In particular, several studies reveal that depression may be characterized along dimensions of negative affect, agitation and hostility, and lassitude and malaise. No research has examined the relationship between these dimensions and neuropsychological function. Towards this end, 133 in patients with unipolar MDD and 17 people without psychiatric illness were administered a brief battery of neuropsychological tests and the MMPI-2. Paralleling earlier research, principal component analysis of the MMPI-2 revealed symptom dimensions of negative affect, agitation, and lassitude and malaise. Multiple regression analyses showed that the negative affect and agitation dimensions accounted for significant variance on measures of executive function, speed of information processing, new learning, dexterity, and overall impairment. Lassitude and malaise failed to correspond with neuropsychological performance. Implications of these data for clinical practice and neural models of MDD are discussed.

1. Introduction

Major depressive disorder (MDD) is among the most common psychiatric disorders (Kessler et al., 2007). Despite the validity and inherent reliability of the diagnostic construct (Joiner et al., 2005), MDD seems to present variably across individuals. For instance, 67% of people with MDD experience simultaneous symptoms of depressed mood and anhedonia, 28% experience depressed mood without anhedonia, and 5% experience anhedonia without depressed mood (Lewinsohn et al., 2003). Rates of other symptoms likewise vary among diagnosed individuals (cf. Ruscio et al., 2007). These variations between depressed patients possess some capacity to predict treatment response, disease characteristics (e.g., neurotransmitter depletion rates), and morbidity (Joiner et al., 2005).

Although MDD is diagnosed categorically (i.e., disorder is present or absent), accumulating evidence implies that this taxonomy is prone to error, and, in turn, may yield less than perfect diagnostic reliability (cf. Brown and Barlow, 2009). In response, some have proposed that depression may be better described according to symptom dimensions rather than discrete individual symptoms (Andrews et al., 2007; Brown and Barlow, 2009; Prisciandaro and Roberts, 2009; Watson, 2009). Indeed, the National Institute of Mental Health recently released proposed Research Domain Criteria for depression, and has specified that research endeavors should assess multiple dimensions of depressive symptoms.

Most of this research implies that a general dimension of negative affect exists, characterized by depressed and anxious mood. Yet, other symptom dimensions may be present (cf. Watson et al., 2007), and multiple dimensional models have been proposed (cf. Brown and Barlow, 2009). Despite their differences, these models have typically included dimensions of negative affect, anhedonia (or low positive emotionality), and some aspect of somatic arousal associated with mood states (e.g., Brown et al., 1998).

For example, Biondi et al. (2005) studied depressive symptom structure among outpatients diagnosed with major depression. They administered the Minnesota Multiphasic Personality Inventory-2 (MMPI-2), and found three dimensions of symptoms. A negative affect dimension consisted of Scales 2 (Depression), 7 (Psychasthenia), 8 (Schizophrenia), and 10 (Social Introversion). Scales 9 (Mania), 6 (Paranoia), and 4 (Psychopathic Deviate)

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comprised an activation and hostility dimension, and scales 3 (Hysteria) and 1 (Hypochondriasis) encompassed a lassitude and physical complaint dimension. Subsequently, Biondi and colleagues replicated these symptom clusters using two separate self-report measures and a different sample of depressed outpatients (Pancheri et al., 2002; Biondi et al., 2005). Moreover, in another investigation (Benazzi, 2001), factors of negative affect, lassitude-malaise, and agitation-activation were observed in depressed outpatients using the Montgomery–Asberg Depression Rating Scale. Furthermore, comparable outcomes were reported in depressed inpatients using a clinician symptom rating scale (Harvey et al., 2009).

These dimensions correspond with clinical observations and theory concerning the psychopathology of MDD (Fava et al., 1991; Bagby et al., 1997; Andrews et al., 2007; Brown and Barlow, 2009; Prisciandaro and Roberts, 2009; Watson, 2009). For instance, some investigators (Watson, 2009) assert that patients with MDD may vary across several symptom dimensions, with depression, anxious arousal, and worry comprising distinct dimensions of distress. They further accord well with findings from the NIMH Collaborative Psychobiology of Depression Study, which found that depressive symptoms may be characterized across at least three independent dimensions; anxiety–agitation; depressed mood-motor retardation, and hostility-interpersonal sensitivity (Katz et al., 1984, 2004).

Paralleling the variable presentation of depressive symptoms, neuropsychological impairment likewise manifests variably across patients. In particular, neuropsychological impairment occurs commonly in MDD, and the most frequent areas of impairment involve executive function, new-learning, working memory, and speed of information processing (e.g., Veiel, 1997; Gualtieri and Morgan, 2009; Clark et al., 2009). Yet, not every depressed patient shows these deficits. Severity of depression, inpatient status, presence of recurrent episodes or psychotic features, co-morbid anxiety, and chronicity of depression are factors that seem to predict increasing neuropsychological morbidity in MDD (e.g., Basso and Bornstein, 1999a; 1999b, 2007). To our knowledge, however, no studies have examined the relationship between dimensions of depressive symptoms and neuropsychological impairment. Research that examines the relationships between these dimensions and neuropsychological function may reveal what depressive factors predict neuropsychological impairment. In doing so, salient morbidity and vulnerability characteristics associated with MDD may be determined, thereby helping clinicians prioritize treatment goals. Moreover, to the extent that specific relationships between symptom dimensions and neuropsychological domains emerge, the data may implicate underlying neural substrates that can be the target of specific interventions.

For instance, a growing literature indicates that MDD corresponds both with hyperactivity in the medial prefrontal cortex and ventral medial striatum, and with hypoactivity in the lateral prefrontal cortex (cf. Drevets et al., 2008; Price and Drevets, 2010). Yet, these general patterns vary among depressed individuals. Indeed, inconsistent manifestations of hyper- and hypoactivation are believed to correspond with the hetereogeneity of MDD symptoms (Drevets et al., 2008). Some researchers have even asserted that the dimensions of negative affect, lassitude, and agitation may correspond with distinct patterns of abnormal cerebral activation involving the ventral, medial, and lateral frontal lobes as well as structures in the medial temporal lobe (cf. Dunn et al., 2002; Ressler and Mayberg, 2007; Carhart-Harris et al., 2008; Price and Drevets, 2010). Although these predictions are compelling, support for them is still nascent, and uncertainties remain. Inasmuch as neuropsychological domains correspond with depressive symptom dimensions, this would lend credence to these emerging neural models of MDD.

Towards this end, the present research sought to examine the relationship between dimensions of depressive symptoms and neuropsychological function in people with MDD. Extending prior studies, which relied exclusively upon outpatients (e.g., Benazzi, 2001; Pancheri et al., 2002; Biondi et al., 2005), the current research recruited only inpatients. This group is apt to present with a greater range of depressive symptoms and is more likely to manifest neuropsychological impairment (e.g., Veiel, 1997). Consistent with earlier research (Biondi et al., 2005), we employed the MMPI-2, and hypothesized three underlying dimensions of depressive symptoms; namely, negative affect, lassitude and physical symptoms, and agitation and hostility. These factors were observed in prior research involving outpatients with MDD (e.g., Biondi et al., 2005). We sought to determine whether these dimensions of depressive symptomatology corresponded with domains of executive function, working memory, new-learning, and dexterity.

2. Method

2.1. Participants

Data were collected retrospectively from the records of 133 inpatients with primary diagnoses of MDD, 32 of whom presented with psychotic features. Owing to potential confounds between unipolar and bipolar depression, patients with bipolar disorder were not enrolled. Patients were administered neuropsychological tests as part of a routine diagnostic evaluation completed during a hospital admission. Patients provided informed consent to neuropsychological testing as part of their treatment plan, and retrospective data collection from medical records was approved under the auspices of the institutional review board. Diagnoses were made during the hospitalization, and drawn from discharge summaries and made in accordance with DSM-IV criteria applied by a board-certified attending psychiatrist at a teaching-hospital. In arriving at a diagnosis, the psychiatrist considered presenting symptoms, diagnostic interviews and chart histories. Although such a diagnostic strategy is not optimal, several studies demonstrate that it yields diagnoses that are reliable, valid, and highly commensurate with those obtained from structured diagnostic interviews (cf. Maziade et al., 1992; Fennig et al., 1994; Warner and Peabody, 1995). No participants had sustained a loss of consciousness or had a history of co-morbid developmental delay or neurologic disease. None of the patients had received electroconvulsive therapy at the time of their hospitalization or testing. Data were also collected from 17 control subjects who were recruited from the community through public notices. All of these participants denied current or previous psychiatric symptoms, diagnoses, or treatment. In screening interviews, they further denied prior loss of consciousness or history of neurological illness. Including the control group permitted us to obtain performance that ranged from normal to abnormal, thereby enhancing sensitivity of the inferential statistics.

The patients with and without psychotic features and control subjects did not differ according to ethnic composition ($\chi^2(2)=0.97$, $p>0.05$). However, a χ^2 test showed that groups did differ in sex composition ($\chi^2(2)=13.55$, $p<0.001$): the control group included no males, but the MDD group was 38% male. According to oneway ANOVAs, the groups did not differ significantly in age ($F(2, 147)=2.65$, $p>0.05$), but they differed in years of education ($F(2, 147)=6.72$, $p<0.002$). Contrasts revealed that the control group had more education than the two patient groups. The patient groups did not differ with regard to prevalence of alcohol ($\chi^2(2)=0.35$, $p>0.05$) or drug abuse disorders ($\chi^2(2)=2.13$, $p>0.05$). Table 1 details sex, ethnicity, and age, and education data for the participant groups. Owing to their potential influence on neuropsychological tests, effects of age, education, and sex were evaluated in the ensuing statistical analyses.

At the time of examination, all but eight of the patients were receiving medication. Date upon which medication commenced was not recorded, but treatment generally began shortly after hospital admission. Because medication may influence cognitive function, we examined whether medication correlated with self-reported symptoms on the MMPI-2 and neuropsychological test performance. Consequently, chlorpromazine equivalent dosages (Jeste and Wyatt, 1982) were calculated for each patient, as were anticholinergic and dopamine blocking ratings and sedation ratings (Arana and Hyman, 1991; Bezchibnyk-Butler and Jeffries, 1991). The analyses revealed no significant relationship between medication ratings and emotional distress or neuropsychological function. None of the correlations exceeded an absolute value of 0.2.

2.2. Procedure

Patients and the control group were administered a brief battery of tests that have demonstrated sensitivity to cerebral dysfunction. Because prior research

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