Journal of Affective Disorders 140 (2012) 48–56

Contents lists available at SciVerse ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research report

The validity of the severity–psychosis hypothesis in depression

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ARTICLE INFO

Article history:
Received 13 October 2011
Received in revised form 25 January 2012
Accepted 26 January 2012
Available online 3 March 2012

Keywords:
Depressive disorder
Major
Affective disorders
Psychotic
Electroconvulsive therapy
Psychiatric Status Rating Scale

ABSTRACT

Background: Psychotic depression (PD) is classified as a subtype of severe depression in the current diagnostic manuals. Accordingly, it is a common conception among psychiatrists that psychotic features in depression arise as a consequence of depressive severity. The aim of this study was to determine whether the severity of depressive and psychotic symptoms correlate in accordance with this "severity–psychosis" hypothesis and to detect potential differences in the clinical features of PD and non-psychotic depression (non-PD).
Methods: Quantitative analysis of Health of the Nation Outcome Scales (HoNOS) scores from all patients admitted to a Danish general psychiatric hospital due to a severe depressive episode in the period between 2000 and 2010 was performed.
Results: A total of 357 patients with severe depression, of which 125 (35%) were of the psychotic subtype, formed the study sample. Mean HoNOS scores at admission differed significantly between patients with non-PD and PD on the items *hallucinations and delusions* (non-PD = 0.33 vs. PD = 1.37, $p<0.001$), *aggression* (non-PD = 0.20 vs. PD = 0.36, $p=0.044$) and on the total score (non-PD = 10.55 vs. PD = 11.87, $p=0.024$). The HoNOS scores on the two items "*depression*" and "*hallucinations and delusions*" were very weakly correlated.
Limitations: Diagnoses were based on normal clinical practice and not formalized research criteria.
Conclusions: The symptomatology of PD and non-PD differs beyond the mere psychosis. Furthermore, severity ratings of depressive and psychotic symptoms are very weakly correlated. These findings offer further support to the hypothesis stating that the psychotic- and non-psychotic subtypes of depression may in fact be distinct clinical syndromes.

1. Introduction

Psychotic depression is currently classified as a subtype of severe depression in both the 10th revision of the International Classification of Disease (ICD-10) (World Health Organization, 1992) and the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (American Psychiatric Association, 2000). Several authors have suggested, that PD should rather be considered and classified as a distinct clinical syndrome on par with non-psychotic depression (non-PD) (Glassman and Roose, 1981; Rothschild, 2009; Schatzberg and Rothschild, 1992). This suggestion is based on a large body of literature, which documents important differences between patients with PD and non-PD. These differences include a more overactive hypothalamic–pituitary–adrenal axis (Holsboer, 2000; Nelson and Davis, 1997; Rothschild et al., 1989; Schatzberg and Rothschild, 1988; Schatzberg et al., 1983) and decreased levels of plasma dopamine-β-hydroxylase (Meltzer et al., 1976; Meyers et al., 1999) in patients with PD compared to non-PD. The symptom-profile of PD is different from that of non-PD, beyond the mere psychosis, with higher prevalence of agitation, rumination, perplexity and cognitive dysfunction (Fleming et al., 2004; Hill et al., 2004; Maj et al., 2007). Regarding treatment, PD has shown a relatively poor response

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doi:10.1016/j.jad.2012.01.039

to placebo (Spiker and Kupfer, 1988), antidepressant monotherapy (Coryell 1998; Glassman and Roose, 1981) and antipsychotic monotherapy (Meyers et al., 2009), but a favorable response to combinations of antipsychotics and antidepressants (Wijkstra et al., 2005, 2010) and to electroconvulsive therapy (ECT) (Loo et al., 2010; Petrides et al., 2001) compared to non-PD. Finally, PD has been associated with increased rates of relapse (Johnson et al., 1991), more psychosocial impairment (Coryell et al., 1996), higher rates of conversion to bipolar disorder (Akiskal et al., 1983), decreased quality of life (Cramer et al., 2010), higher risk of suicide (Wenzel et al., 2011) and higher mortality rates compared to non-PD (Vythilingam et al., 2003).

It is a common conception among psychiatrists that psychotic features in depression arise as a consequence of depressive severity. The existence of such a "severity–psychosis" relationship is supported by some studies (Bellini et al., 1992; Lattuada et al., 1999; Parker, 2011), and also implicitly underlies the classification of depression in both the DSM-IV-TR (American Psychiatric Association, 2000) and the ICD-10 (World Health Organization, 1992), where PD can only be classified under severe depression. However, recent studies have demonstrated that episodes of PD are not necessarily "severe" as judged by the number of depressive symptoms (Maj, 2011; Maj et al., 2007; Ohayon and Schatzberg, 2002). Furthermore, patients with no history of psychotic symptoms may experience non-psychotic depressive episodes of greater symptom-severity than the psychotic depressive episodes experienced by patients with PD (Forty et al., 2009).

The aim of the present study was to subject the severity–psychosis hypothesis of depression to a quantitative analysis and to detect potential clinical differences between patients diagnosed with PD and non-PD respectively. More specifically, we aimed to answer the following questions:

- Does the severity of depression and psychosis correlate among patients with severe unipolar depression?
- Does the symptom profile of hospitalized patients with PD and non-PD differ at admission and discharge?
- Are patients with PD and non-PD equally likely to receive ECT and do they respond to this treatment to the same extent? What characterizes patients elected for ECT?

2. Methods

The data for the present study was collected at Psychiatric Center Nordsjælland, Hillerød, Denmark — a general psychiatric hospital with 170 beds, covering a catchment area of approximately 370.000 people. Since January 2000 clinical data has been collected consecutively from all patients admitted to the hospital for more than 48 h. The study was approved by the Danish Data Protection Agency and the Danish Board of Health. The database contains the following information:

2.1. ICD-10 diagnoses

As part of routine clinical practice at Danish psychiatric hospitals, patients are assigned with diagnoses according to the ICD-10 by the treating psychiatrist. Several diagnoses can be assigned, but only the main-diagnosis was recorded in the clinical database used in this study. Patients assigned with main-diagnoses of severe unipolar depression (F32.2, F32.3, F33.2 and F33.3) between January 1st 2000 and December 31st 2010 constituted the study sample. Only the first admission with severe depression within the study period was considered. The patients were divided into non-PD (F32.2 and F33.2) and PD (F32.3 and F33.3) in accordance with the ICD-10 subtyping of severe depression.

2.2. HoNOS-ratings at admission and discharge

Patients were rated on the Health of Nation Outcome Scale (HoNOS) (Wing et al., 1998). HoNOS was developed in 1993 by the Royal College of Psychiatrists on a commission from the UK Department of Health. The scale measures the behavior, impairment, symptoms and social functioning of patients with severe mental illness and contains 12 items: *Aggression*, *Self-harm*, *Drug or alcohol use*, *Cognitive problems*, *Physical illness and disability*, *Hallucinations and delusions*, *Depression*, *Other mental and behavioral problems*, *Problems with relationships*, *Problems with activities of daily living*, *Problems with living conditions*, and *Problems with occupation and activities*. Each item is rated on a five-point Likert scale: 0 = no problem, 1 = minor problem requiring no action, 2 = mild problem but definitely present, 3 = moderately severe problem, 4 = severe to very severe problem. The scale has mainly been used in English speaking countries (Duke, 2010; Fisher et al., 2004; Trauer et al., 1999) but several studies have been published using translated versions in French (Lauzon et al., 2001), German (Andreas et al., 2007), Italian (de Girolamo et al., 2005; Morlino et al., 2011; Tomasi et al., 2005) and Danish (Bech et al., 2003, 2006). Total- and individual HoNOS item-scores have proven to be valid measures for a number of outcomes in varying settings: assessing reliable and clinically significant change under admission (McClelland et al., 2000; Parabiaghi et al., 2005); rating suicidality in schizophrenia (Hansen and Kingdon, 2006); rating severity of mental illness in consultant liaison psychiatry (Duke, 2010); measuring symptom severity in patients with substance-related disorders (Andreas et al., 2010), depression (Newnham et al., 2010) and psychosis (Amin et al., 1999); assessing outcome in community mental health patients (Parker et al., 2002); identifying frequently hospitalized patients and ranking mental disorders according to the ICD-10 hierarchy (Bech et al., 2006). In the present study, rating was performed by the nursing staff based on a semi-structured interview, conducted within 48 h from admission and again at discharge. The inter-staff agreement on the HoNOS was not assessed in relation to this study, but has previously been found acceptable in a study conducted at the same hospital (Bech et al., 2006).

2.3. Electroconvulsive therapy

If patients received ECT during their admission it was recorded in the database. The number, frequency and stimulus intensity of the treatments was not specified. ECT was applied using the Thymatron System IV. In most cases, patients received 3 treatments per week. The electrode placement was bifrontotemporal for the first 3 treatments, followed by