Journal of Affective Disorders 155 (2014) 35–41

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research report

Dimensions in major depressive disorder and their relevance for treatment outcome

Elske Vrieze [a,*], Koen Demyttenaere [a], Ronny Bruffaerts [a], Dirk Hermans [b], Diego A. Pizzagalli [c], Pascal Sienaert [d], Titia Hompes [a], Peter de Boer [e], Mark Schmidt [e], Stephan Claes [a]

[a] Department of Psychiatry, University Psychiatric Center, Campus Leuven, Leuven, Belgium
[b] Department of Psychology, KU Leuven, Leuven, Belgium
[c] Department of Psychiatry, Harvard Medical School, Belmont, MA, USA
[d] Department of Psychiatry, University Psychiatric Center, Campus Kortenberg 3070, Belgium
[e] Janssen Research and Development, Division of Janssen Pharmaceutica, NV, Beerse, Belgium

ARTICLE INFO

Article history:
Received 26 August 2012
Received in revised form
11 October 2013
Accepted 12 October 2013
Available online 19 October 2013

Keywords:
Major depressive disorder
Factor analysis
Anhedonia
Stress
Outcome

ABSTRACT

Background: Major depressive disorder (MDD) is a heterogeneous disease. More homogeneous psycho (patho)logical dimensions would facilitate MDD research as well as clinical practice. The first aim of this study was to find potential dimensions within a broad psychopathological assessment in depressed patients. Second, we aimed at examining how these dimensions predicted course in MDD.
Methods: Ten psychopathological variables were assessed in 75 MDD inpatients. Factor and regression analyses assessed putative relations between psychopathological factors and depression severity and outcome after 8 weeks of treatment.
Results: A 3-factor model (eigenvalue: 54.4%) was found, representing a psychomotor change, anhedonia and negative affect factor. Anhedonia and negative affect predicted depression severity ($R^2=0.37$, $F=20.86$, $p<0.0001$). Anhedonia predicted non-response (OR 6.00, CI 1.46–24.59) and both negative affect (OR 5.69, CI 1.19–27.20) and anhedonia predicted non-remission (OR 9.28, CI 1.85–46.51).
Limitations: The sample size of the study was relatively modest, limiting the number of variables included in the analysis.
Conclusions: Results confirm that psychomotor change, anhedonia and negative affect are key MDD dimensions, two of which are related to treatment outcome.

1. Introduction

Current neurobiological and behavioral research on the psychopathology of Major depressive disorder (MDD), as well as common clinical practice, increasingly considers MDD as a multidimensional and heterogeneous concept (Hasler et al., 2004; Zimmerman, 2009). Affected individuals are associated with a wide variety of risk factors, symptoms and other clinically relevant variables, such as demographic characteristics, comorbidity, personality traits and characteristics of depressive episodes (Kendler, 1999). A data-driven approach to identify meaningful components or latent dimensions within a heterogeneous diagnostic construct is factor analysis (Comrey et al., 1978). In the past, several studies have used factor analytic strategies to identify subdimensions of MDD, based on clinical rating scales for depression and other symptom measures reflecting DSM-IV criteria (e.g., Carragher et al., 2009; Cassano et al., 2009; Harald and Gordon, 2012). The most commonly identified factors in MDD are a depression severity factor and a somatic factor (Shafer, 2006). A few studies report a positive affect factor and a psychomotor factor (Schrijvers et al., 2008).

However, most of the studies using factor analysis in MDD research have important limitations. First, the proposed factors have been largely limited to clinical symptoms without attempts to correlate the factors with variables across different units of analysis, such as etiological characteristics of MDD. Classifying psychopathology based on dimensions of observable behavior, risk factors as well as psychobiological measures would define dimensions on their basic functions and cutting across categorical disorders as traditionally defined. It seems clear that clusters of self-reported symptoms is constraining advances in understanding the pathophysiology of mental illnesses and in addition hampers the development of better treatments (Insel and Charney, 2003). Second, the clinical relevance in terms of the influence of these

* Correspondence to: Department of Psychiatry, University Psychiatric Center, campus Kortenberg, Belgium, Sint Jozef hospital. Leuvensesteenweg 517, 3070 Kortenberg, Belgium. Tel.: +32 27580867.
E-mail addresses: elske.vrieze@uc-kortenberg.be, elske_vrieze@hotmail.com (E. Vrieze).

0165-0327/$ - see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.jad.2013.10.020

factors on outcome in MDD patients has often not been examined in detail. Identifying reliable predictors of outcome in research may allow for the development of novel and more specified interventions (Chen et al., 2000; Insel et al., 2010).

The primary effort of this study was to discover basic dimensions of functioning within MDD, by including variables across different units of analysis, from core MDD symptoms to potentially important underlying risk factors and behaviors. In addition, we evaluated the clinical relevance of these dimensions by investigating their relation to depression severity and their ability to predicting outcome.

To achieve our aims, we conducted a factor analysis based on a broad range of psychopathological characteristics, assessed in 75 depressed inpatients. Ten clinical symptoms of MDD, as well as additional features representing underlying psychopathological vulnerability and environmental factors involved in the development of MDD were included in the factor analysis. In an additional analysis, potential latent dimensions were evaluated with regard to their relationship to outcome after 8 weeks of treatment using logistic regression models. Outcome was operationalized using response and remission rates.

2. Materials and methods

2.1. Participants

Eighty-two depressed patients participated in this study. All patients were hospitalized at the University Psychiatric Center of the University of Leuven, Belgium. The Structured Clinical Interview for DSM-IV-TR (SCID-I) (Spitzer et al., 1992) was used to make DSM-IV diagnoses of MDD. Patients with other mood spectrum disorders, addiction, psychotic disorders or any other unstable medical condition were excluded. All patients received pharmacological and/or psychotherapy treatment, as clinically appropriate. All participants signed an informed consent and the local ethics committee approved the study.

2.2. Design and procedures

This investigation was part of a larger longitudinal study, examining potential endophenotype in MDD, which provided the sample used to test the current hypothesis. Endophenotype research attempts to define an heterogeneous phenotype of a disease with more homogeneous subdimensions based on psychopathology, biology and genes (Hasler et al., 2004). In the longitudinal study, signs and symptoms were chosen based on their specificity and/or clinical and biological plausibility with regards to two potential endophenotypes recently described in MDD: anhedonia and increased stress sensitivity (Vrieze and Claes, 2009). The data on reward responsiveness used in this study has recently been published in an other paper pursuing a different research aim (Vrieze et al., 2013).

The selection of instruments used in this protocol was chosen to capture key symptom patterns, risk factors and etiological underpinnings of MDD. We limited the number of variables to 10 due to our relative small sample size. All patients were evaluated within the first week of admission. After 8 weeks, a follow-up appointment was made and response and remission measurements were taken. All measures and ratings were completed by a psychiatrist (E.V.) or trained psychiatric research nurse.

2.3. Data collection and reduction

2.3.1. Clinical assessments and measures

Key emotional symptoms of MDD were measured using the positive and negative affect scale (PANAS) (Davidson, 2003; Watson et al., 1995). This 20-item self-rating scale rates negative affect (NA), which represents features such as distress and anxiety, and positive affect (PA), which entails features such as feeling happy, energetic and alert (Watson et al., 1988). Since anhedonia is a specific, core feature and potential endophenotype of MDD (Hasler et al., 2004), subjects also completed the Snaith–Hamilton pleasure scale (SHAPS) (Snaith et al., 1995). The SHAPS is a 14-item questionnaire probing participants' hedonic capacity in a variety of situations (Franken et al., 2007). The CORE assessment of psychomotor change (CORE) was included to assess psychomotor changes (Parker et al., 1994). The CORE scale is specifically designed to differentiate between melancholic and non-melancholic depression and rates 18 observable features in 3 dimensions: non-interactiveness (e.g., inattentiveness, poverty of associations, impaired spontaneity of talk), retardation (e.g., facial immobility, postural slump, delay in verbal response, slowed speech) and agitation (e.g., facial apprehension and agitation, stereotype movements). Before utilizing the CORE-scale, raters were trained by studying the information video and role-playing. Participants completed the NEO-five factor inventory (NEO-FFI) to obtain a measure of the personality dimension neuroticism (Costa and McCrae., 1992), which is considered the most important predisposing personality dimension for MDD (Kendler et al., 2004). The NEO-FFI measures neuroticism by exploring personality aspects of anxiety, irritation, depression, shame, impulsivity, and vulnerability. Only the neurotic subscale of the NEO-FFI was used in this study. The semi-structured trauma questionnaire (STI) was included to assess early life stress (ELS) (Draijer and Langeland, 1999). Environmental factors play an important role in MDD and it is generally assumed that stress is key feature in the etiology of MDD (Kessler, 1997). The trauma interview focuses on assessing severity of childhood experience with sexual and physical violence and early parental separation. Early parental separation is coded positively when subjects are separated from one or both parents for more than 6 months, before the age of 12. Mild ELS is coded when subjects experienced mild physical or sexual trauma before the age of 16. Severe ELS is coded when subjects experienced severe sexual trauma, severe physical trauma or both, before the age of 16. Coding of the interviews was performed by one trained rater. The 17-item Hamilton depression rating scale (HDRS) (Hamilton, 1960) assessed severity of MDD at baseline. The HDRS was repeated 8 weeks following study entry to evaluate both non-response and non-remission rates. Response was defined as a 50% improvement on the HDRS after 8 weeks. Remission was defined as a score of ≤ 7 on the HDRS at 8 weeks.

2.3.2. Reward task

We used a computerized reward learning task to measure reward responsiveness. Reduced reward responsiveness is hypothesized to be an important mechanism in the development of MDD (Eshel and Roiser, 2010). The task relies on signal-detection theory in which correct identifications of two stimuli were differentially rewarded. In 300 trials, divided in 3 blocks of 100 trials, two difficult-to-discriminate stimuli were briefly (100 ms) presented an equal number of times. The participants' task was to win as much money as possible by accurately identifying which stimulus was presented after each trial. To induce a response bias, an asymmetrical reinforcer schedule was used, such as correct responses for one stimulus (referred to as the 'rich') were rewarded three times more frequently than correct responses of the other stimulus (referred to as the 'lean'). Due to the unequal frequency of reward feedback, participants with high reward responsiveness were expected to develop a response bias in favor of the rich stimulus compared to the lean stimulus over the course of the 3 blocks. Subjects with low reward