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Research paper

# A personality-based latent class typology of outpatients with major depressive disorder: association with symptomatology, prescription pattern and social function

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ABSTRACT

*Background:* While major depressive disorder (MDD) is considered to be a heterogeneous disorder, the nature of the heterogeneity remains unclear. Studies have attempted to classify patients with MDD using latent variable techniques, yet the empirical approaches to symptom-based subtyping of MDD have not provided conclusive evidence. Here we aimed to identify homogeneous classes of MDD based on personality traits, using a latent profile analysis.

*Methods:* We studied 238 outpatients with DSM-IV MDD recruited from our specialized depression outpatient clinic and assessed their dimensional personality traits with the Temperament and Character Inventory. Latent profile analysis was conducted with 7 dimensions of the Temperament and Character Inventory as indicators. Relationships of the identified classes with symptomatology, prescription pattern, and social function were then examined.

*Results:* The latent profile analysis indicated that a 3-class solution best fit the data. Of the sample, 46.2% was classified into a "neurotic" group characterized by high harm avoidance and low self-directedness; 30.3% into an "adaptive" group characterized by high self-directedness and cooperativeness; and 23.5% into a "socially-detached" group characterized by low reward dependence and cooperativeness and high self-transcendence. The 2 maladaptive groups, namely neurotic and socially-detached groups, demonstrated unique patterns of symptom expression, different classes of psychotropic medication use, and lower social functioning.

*Limitations:* Generalizability of the findings was limited since our patients were recruited from the specialized depression outpatient clinic.

*Conclusions:* Our personality-based latent profile analysis identified clinically meaningful 3 MDD groups that were markedly different in their personality profiles associated with distinct symptomatology and functioning.

## 1. Introduction

Major depressive disorder (MDD) is now widely viewed as a multifactorial and heterogeneous disorder through the accumulation of scientific evidence. Patients with MDD can vary greatly in clinical presentation, treatment response, and etiological factors. This is not surprising given that the formal diagnosis of MDD is made based solely on clinical symptoms and that there are a large number of possible combinations of symptoms within MDD (APA, 2013). Such heterogeneity not only impedes the progress of research into the pathophysiology of MDD but poses a significant challenge to clinical practice. Although several theoretically derived subtypes of MDD have been proposed based on differences in characteristic symptoms (e.g., melancholic, atypical, psychotic), onset/course (e.g., early- vs. late-life, seasonal, postpartum, single vs. recurrent, chronic) and illness severity, their clinical relevance has been questioned (Rush, 2007).

Recently, data-driven approaches have been used in an attempt to overcome this issue. A latent class analysis (LCA) is an empirically-derived, person-centered statistical method to classify individuals based on a set of observed response variables. LCA is thus used to

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uncover unobserved heterogeneity in a population and identify homogeneous subgroups. For clustering purposes, cluster analysis methods (hierarchical and non-hierarchical clustering) based on a distance measure of dissimilarity have long been used; however, they have been increasingly complemented by probabilistic modeling methods including LCA. An important practical advantage of LCA over cluster analysis is that it is a data-driven clustering technique where the optimal number of classes is determined based on information criteria and likelihood ratio tests. However, previous studies applying LCA to symptomatology of depression have only yielded subgroups with different overall severity but not qualitatively distinct subtypes based on symptom profiles (reviewed in van Loo et al., 2012). This may be related to the fact that symptoms can fluctuate over time within an individual, and therefore, LCA studies that go beyond symptomatology and explore MDD subtypes according to other important aspects of depression would be needed.

It has increasingly been recognized that diagnosis and research in psychiatry should turn its attention to the underlying causes rather than surface symptoms (Insel and Cuthbert, 2015). Since MDD is a moderately heritable disorder (Sullivan et al., 2000) where many susceptibility genes with small effects are thought to play a role, some endophenotypic markers that mediate genetic effects on the disease phenotype could be useful (Gottesman and Gould, 2003). Personality is one of such candidates, as they are to some extent genetically determined (Okbay et al., 2016) and are involved in the development of depressive disorders (Akiskal et al., 1983). Personality traits have also been shown to predict treatment response in MDD patients (Kaneda et al., 2011; Quilty et al., 2008). Given that different personality traits are considered to interact within an individual (Markon et al., 2005) and that any single trait can have both advantages and disadvantages depending on the context (Ferguson et al., 2014), LCA of dimensional personality traits will represent an effective approach in searching for subtypes of MDD that are clinically and etiologically relevant.

Among various tools designed to assess dimensional personality traits, the Temperament and Character Inventory (TCI; Cloninger et al., 1993) is one of the most commonly used self-report questionnaires. By measuring an array of personality dimensions, the TCI accounts for both normal and abnormal personality variations (Cloninger et al., 1993). Compared to healthy controls, patients with MDD have been associated with significant alterations in most personality dimensions assessed by the TCI (Farmer et al., 2003; Sasayama et al., 2011), some of which remain altered even after remission is achieved (Richter et al., 2000; Teraishi et al., 2015). Furthermore, specific dimensions of the TCI have been shown to sensitively distinguish between bipolar vs. unipolar depression (Evans et al., 2005; Sasayama et al., 2011) and between remitted patients with single vs. recurrent episode (Richter et al., 2000; Teraishi et al., 2015).

The present study aimed to find latent homogeneous classes of MDD based on temperament and character, using LCA. We further attempted to validate the identified latent classes by symptomatology, prescription pattern and social functioning. Additionally, symptom-based latent classes were also examined, and their relation to the personality-based latent classes was explored. Our hypotheses were that (1) LCA would identify at least 3 qualitatively different MDD subtypes according to unique personality profiles, (2) the identified different subtypes would be each associated with distinct clinical features and/or functional status, such that those suptypes with less adaptive personality profiles would be characterized by more severe symptoms and lower functioning, and (3) the personality-based latent classes would reveal different aspects of MDD subtypes from those revealed by the symptom-based latent classes.

## 2. Methods

### 2.1. Participants

A total of 238 patients with DSM-IV MDD (age range: 16–76 years; 82 women) were recruited from our specialized depression outpatient clinic of the National Center of Neurology and Psychiatry (NCNP) Hospital, Tokyo, Japan. Many of these patients had suffered from prolonged depression despite previous treatment attempts and were referred to our clinic in order to receive comprehensive diagnostic assessment and intensive treatment for their refractory depressive illness. Clinical diagnosis was made by an experienced psychiatrist based on interviews, observations and case notes. This diagnosis was confirmed using the mood disorders module of the Structured Clinical Interview for DSM-IV (SCID) Axis-I disorders (First et al., 1997) by a research psychiatrist. These interview-based clinical assessments were made independently of the self-reported personality measure (i.e., TCI). Of the 238 patients with MDD, 29 were diagnosed as having comorbid dysthymic disorder based on the SCID. Patients with bipolar disorder were excluded. Of the patients, 4 were clinically diagnosed as having comorbid anxiety disorders (2 of them had panic disorder), and 5 as having comorbid personality disorders (3 of them had borderline personality disorder). The type (i.e., single vs. recurrent) of major depressive episode was determined in 198 (83.2%) patients. Additional exclusion criteria included a history of central nervous system diseases or severe head injury, or current substance abuse/dependence. The present study was approved by the ethics committee of the NCNP, and was conducted in accordance with the Declaration of Helsinki. After description of the study, written informed consent was obtained from every participant (or his/her parent when the participant was minor).

### 2.2. Measures

Psychological/clinical measures were used to assess symptomatology, personality, and global/social functioning. All these assessments were made at the first visit to the clinic.

Depressive symptoms were assessed by the GRID-Hamilton Depression Rating Scale 21-item version (HAMD-21; Hamilton, 1967). Total scores of 14–18 on its 17-item version are considered to indicate moderate depression. In addition to the overall illness severity as indexed by the total score, different symptom dimensions were evaluated by its subscales.

The validated Japanese version (Kijima et al., 1996, 2000) of the TCI (Cloninger et al., 1993) was used for personality assessment. The TCI is a 240-item (including 14 items that are not analyzed) self-report questionnaire, with each item requiring a true/false answer. Temperament refers to automatic emotional and behavioral reactions to subjective experiences that are assumed to be genetically transmitted and therefore stable over time. Four dimensions of temperament are distinguished: novelty seeking, harm avoidance, reward dependence, and persistence. Novelty seeking consists of 40 items that are classified into 4 subscales, including exploratory excitability, impulsiveness, extravagance, and disorderliness. Harm avoidance comprises 35 items classified into 4 subscales, including anticipatory worry, fear of uncertainty, shyness with strangers, and fatigability and asthenia. Reward dependence comprises 24 items classified into 3 subscales, including sentimentality, attachment, and dependence. Persistence comprises 8 items classified into a single subscale of persistence. Character refers to individual differences in higher cognitive processes such as intentions, decisions and values. Three dimensions of character are distinguished: self-directedness, cooperativeness, and self-transcendence. Self-directedness comprises 44 items classified into 5 subscales, including responsibility, purposefulness, resourcefulness, self-acceptance, and congruent second nature. Cooperativeness comprises 42 items classified into 5 subscales, including social acceptance, empathy, helpfulness, compassion, and integrated conscience. Self-