New Dimensions in the Quantitative Classification of Mental Illness

Roman Kotov, PhD; Camilo J. Ruggero, PhD; Robert F. Krueger, PhD; David Watson, PhD; Qilong Yuan, PhD; Mark Zimmerman, MD

Context: Patterns of comorbidity among mental disorders are thought to reflect the natural organization of mental illness. Factor analysis can be used to investigate this structure and construct a quantitative classification system. Prior studies identified 3 dimensions of psychopathology: internalizing, externalizing, and thought disorder. However, research has largely relied on common disorders and community samples. Consequently, it is unclear how well the identified organization applies to patients and how other major disorders fit into it.

Objective: To analyze comorbidity among a wide range of Axis I disorders and personality disorders (PDs) in the general outpatient population.

Design: Clinical cohort study.

Setting: A general outpatient practice, the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project.

Participants: Outpatients (N=2900) seeking psychiatric treatment.

Main Outcome Measures: The Structured Clinical Interview for DSM-IV and the Structured Interview for DSM-IV Personality.

Results: We tested several alternative groupings of the 25 target disorders. The DSM-IV organization fit the data poorly. The best-fitting model consisted of 5 factors: internalizing (anxiety and eating disorders, major depressive episode, and cluster C, borderline, and paranoid PDs), externalizing (substance use disorders and antisocial PD), thought disorder (psychosis, mania, and cluster A PDs), somatoform (somatoform disorders), and antagonism (cluster B and paranoid PDs).

Conclusions: We confirmed the validity of the 3 previously found spectra in an outpatient population. We also found novel somatoform and antagonism dimensions, which this investigation was able to detect because, to our knowledge, this is the first study to include a variety of somatoform and personality disorders. The findings suggest that many PDs can be placed in Axis I with related clinical disorders. They also suggest that unipolar depression may be better placed with anxiety disorders than with bipolar disorders. The emerging quantitative nosology promises to provide a more useful guide to clinicians and researchers.
identified 2 subgroups within the internalizing spectrum: a distress cluster (consisting of major depressive disorder, dysthymic disorder, generalized anxiety disorder, and posttraumatic stress disorder) and a fear cluster (panic disorder, obsessive-compulsive disorder, and phobic disorders). However, these clusters are so highly correlated that they do not emerge as separate elements within the internalizing spectrum.17,18

This research produced valuable insights into the natural organization of mental illness, but it has been limited in 2 respects. First, most studies of adults have been restricted to community samples. Findings of general population surveys do not necessarily generalize to clinical samples. Indeed, it is unclear how well the identified organization applies to psychiatric patients. Factor-analytic studies have begun examining specific patient populations, namely, self-identified patients, treatment-seeking veterans, and inpatients with psychosis.11,19,20 The present investigation sought to extend this work by evaluating a general outpatient sample.

Second, the existing literature focused on common diagnoses, namely SUDs, anxiety and depressive disorders, and antisocial personality disorder (PD). It is uncertain whether the previously identified spectra will be confirmed when a broader range of diagnoses is considered and whether additional dimensions are needed to capture less-common disorders. Several investigations have sought to extend the 2-spectrum model. One21 reported that symptoms of somatization and hypochondriasis belong to the internalizing cluster, although they are less central to it than anxiety and depression. Another study21 found that eating disorders are part of the internalizing spectrum. A third investigation20 observed that schizophrenia and schizotypal PDs form a distinct thought disorder spectrum. Finally, borderline PD was linked to both internalizing and externalizing dimensions.22,23 These findings require replication but suggest hypotheses for the present study.

Other factor-analytic investigations have examined comorbidity among PDs. O'Connor24 cumulated data from 33 studies and found support for 2 structures. The first model consisted of dimensions that can be identified as externalizing (composed of cluster B and paranoid PDs) and internalizing (cluster C, cluster A, and borderline). The second model included the same externalizing factor but split the cluster A PDs—disorders linked to the thought disorder dimension—from the other internalizing conditions. Thus, factor analyses of PDs appear to replicate the spectra found in studies centered on Axis I disorders.

However, only joint analyses of Axis I and Axis II disorders can link the 2 sets of findings. Few such investigations have been undertaken. Beyond antisocial PD, there are some initial data on borderline and schizotypal diagnoses, but virtually nothing is known about placebos. Various Axis I and II symptoms in a British community sample and found 4 broad dimensions: internalizing, externalizing, thought disorder (symptoms of psychosis and cluster A PDs), and pathological introversion (symptoms of avoidant and dependent PDs). It appears that the first 3 dimensions cut across Axis I and Axis II symptomatology, whereas pathological introversion is specific to the latter axis. It is uncertain, however, whether the same dimensions would be found in analyses of the corresponding disorders.

The aim of the present investigation was to broaden the quantitative nosology by examining a wide range of Axis I and Axis II conditions, many of which have not been considered in this framework. In particular, we sought to integrate personality pathology fully into this system and to explicate the nature of the relations between the axes. Moreover, we planned to evaluate the generalizability of the previously identified spectra to the outpatient population using a large, unselected sample diagnosed with state-of-the-art procedures. We hypothesized that the current DSM-IV organization of disorders would fit the data poorly. We further predicted that the internalizing, externalizing, and thought disorder spectra would be confirmed in this sample. We also planned to test whether the same spectra cut across Axis I and Axis II. Finally, we sought to examine the distinction between fear and distress disorders observed within the internalizing cluster in several studies.6,11,15,16 Given that the present analyses go well beyond previous research, we made modifications to our a priori models when such changes were clearly indicated by the data.

METHODS

SAMPLE AND PROCEDURE

Data were obtained from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project, a clinical program created to integrate research assessments into routine care.25 Participants presenting at a community-based outpatient psychiatric practice underwent a comprehensive diagnostic assessment. The practice predominantly treats individuals with medical insurance (including Medicare) on a fee-for-service basis. The main referral sources are primary care physicians, psychotherapists, and family members or friends. All individuals seeking treatment at this practice were asked to participate in the MIDAS project. Exclusion criteria were age younger than 18 years, inability to understand English, and severe cognitive impairment. Nonparticipants were compared with participants using self-administered symptom inventories, and no significant differences were found, suggesting that this sample is representative of the population served by the clinic with regard to psychopathology.17,28 The Rhode Island Hospital's institutional review board approved the research protocol, and all participants provided written informed consent.

The sample included the 2900 consecutive patients evaluated in the MIDAS project since it began. Their mean (SD) age was 38.5 (13.0) years; the majority were female and white (Table 1). Of these patients, 2151 completed the PD assessment. This component was not introduced until the study was under way and the procedures for incorporating research interviews into clinical practice had been well established. As a result, 749 participants were missing PD data. There were no significant differences between participants with and those without PD assessment on any demographic characteristics or Axis I diagnoses except that the latter were more likely to have a psychotic disorder (12.3% vs 6.7%, P < .001) and less likely to have generalized anxiety disorder (18.8% vs 30.6%, P < .001). Thus, missing data likely had little systematic effect on the results. We addressed missing
data with the Full Information Maximum Likelihood method, which uses all available information without deleting any records and is recommended for such missing data patterns.

MEASURES

Lifetime Axis I diagnoses were made using the Structured Clinical Interview for DSM-IV (SCID), which was modified to relax certain hierarchical exclusion rules and thus allow some nonhierarchical diagnoses. Lifetime rather than current diagnoses were chosen for consistency with the PD assessment. Axis II conditions were measured with the Structured Interview for DSM-IV Personality (SIDP). Each DSM-IV PD criterion was rated on a 0 (not present) to 3 (strongly present) scale, with a score of 2 (present) or higher considered positive. The SIDP questions are grouped thematically to reduce halo effects (i.e., ratings for a criterion are influenced by how other criteria of that diagnosis are rated).

Both assessments were administered by highly trained interviewers (including C.J.R.) who were monitored throughout the study to minimize rater drift. Interviewers typically were PhD-level psychologists. Every diagnostician underwent extensive training lasting 3 to 4 months. The raters were required to demonstrate exact agreement with a senior diagnostician on 5 consecutive evaluations. Ongoing supervision by one of the investigators (M.Z.) included weekly case conferences and review of written reports and item ratings of every case. Fourteen raters performed joint interviews to assess the diagnostic reliability of the SCID (based on 65 participants) and SIDP (based on 47 participants). The SCID reliability estimates (κ) ranged from 0.64 to 1.00 (median, 0.88). Reliability of any PD on the SIDP was 0.90. Individual disorders were too rare to be analyzed; thus, the intraclass correlation coefficients for criterion counts ranged from 0.82 to 0.97 (median, 0.94).

The SIDP covers 7 DSM-IV sections: SUDs and mood, psychotic, anxiety, somatoform, adjustment, and eating disorders. In selecting variables for the analyses, we considered both frequency and hierarchical exclusion rules. Disorders with low frequency (defined as <20 cases) were excluded because their associations with other variables were estimated reliably. Diagnoses affected by hierarchical rules could not be analyzed because those rules prohibit certain combinations of diagnoses and therefore would dictate the structure, leading to spurious findings.

Consequently, we examined mood episodes (major depressive and manic) rather than mood disorders, as these diagnoses contain exclusion rules. We used a nonhierarchical generalized anxiety disorder diagnosis. Psychosis—defined as the presence of definite psychotic symptoms, including psychosis during mood episodes—was analyzed as a single category and could not be subdivided because individual psychotic disorders incorporate complex hierarchical rules. For the same reason, we examined a broad eating-disorder group that consisted of anorexia nervosa, bulimia nervosa, and binge eating disorder. In addition, the undifferentiated somatoform disorder group included cases with somatization disorder, which represents an extreme form of this condition. Body dysmorphic disorder was too infrequent to be analyzed. Adjustment disorders were not considered because all involved hierarchical rules that could not be relaxed. Not otherwise specified diagnoses were not counted in any of the categories. Overall, 15 Axis I conditions were selected (Table 1).

The SIDP assesses all 10 PDs, but several diagnoses had low frequency. To ensure comprehensive coverage of personality pathology, we expanded PD categories to include subthreshold cases. Specifically, we required 1 criterion less than DSM-IV thresholds and thus were able to analyze all 10 resulting PD conditions and thus were able to analyze all 10 resulting PD

Table 1. Demographic Characteristics and Diagnoses of the Analysis Sample

<table>
<thead>
<tr>
<th>Race</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>White</td>
<td>2538 (87.5)</td>
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<tr>
<td>Black</td>
<td>128 (4.4)</td>
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<tr>
<td>Other</td>
<td>234 (8.1)</td>
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<table>
<thead>
<tr>
<th>Marital status</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Never married</td>
<td>910 (31.4)</td>
</tr>
<tr>
<td>Married/cohabiting</td>
<td>1359 (46.9)</td>
</tr>
<tr>
<td>Formerly married</td>
<td>631 (21.8)</td>
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<table>
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<tr>
<th>Educational level</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Graduated college or more</td>
<td>829 (28.3)</td>
</tr>
<tr>
<td>Graduated high school</td>
<td>1813 (62.5)</td>
</tr>
<tr>
<td>&lt;High school</td>
<td>267 (9.2)</td>
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<table>
<thead>
<tr>
<th>Sex</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Male</td>
<td>1132 (39.0)</td>
</tr>
<tr>
<td>Female</td>
<td>1768 (61.0)</td>
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<tr>
<th>Axis I conditions</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Psychosis</td>
<td>236 (8.1)</td>
</tr>
<tr>
<td>Manic episode</td>
<td>96 (3.3)</td>
</tr>
<tr>
<td>Major depressive episode</td>
<td>2100 (72.4)</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>799 (27.6)</td>
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<tr>
<td>Posttraumatic stress disorder</td>
<td>610 (21.0)</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>721 (24.9)</td>
</tr>
<tr>
<td>Social phobia</td>
<td>883 (30.4)</td>
</tr>
<tr>
<td>Specific phobia</td>
<td>337 (11.6)</td>
</tr>
<tr>
<td>Obsessive-compulsive disorder</td>
<td>258 (8.9)</td>
</tr>
<tr>
<td>Eating disorder</td>
<td>224 (7.7)</td>
</tr>
<tr>
<td>Undifferentiated somatoform disorder</td>
<td>97 (3.3)</td>
</tr>
<tr>
<td>Hypochondriasis</td>
<td>35 (1.2)</td>
</tr>
<tr>
<td>Pain disorder</td>
<td>37 (1.3)</td>
</tr>
<tr>
<td>Alcohol use disorder</td>
<td>1159 (40.0)</td>
</tr>
<tr>
<td>Drug use disorder</td>
<td>735 (25.3)</td>
</tr>
<tr>
<td>Schizoid</td>
<td>55 (2.6)</td>
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<tr>
<td>Schizotypal</td>
<td>28 (1.3)</td>
</tr>
<tr>
<td>Antisocial</td>
<td>258 (9.6)</td>
</tr>
<tr>
<td>Conduct problems</td>
<td>171 (9.5)</td>
</tr>
<tr>
<td>Borderline</td>
<td>449 (16.1)</td>
</tr>
<tr>
<td>Histrionic</td>
<td>53 (2.5)</td>
</tr>
<tr>
<td>Narcissistic</td>
<td>80 (3.7)</td>
</tr>
<tr>
<td>Dependent</td>
<td>84 (3.9)</td>
</tr>
<tr>
<td>Obsessive-compulsive</td>
<td>343 (15.9)</td>
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a Diagnoses are not mutually exclusive.
b Because of missing data, the prevalence of these conditions was estimated for available cases.

No. (%)       |
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<tbody>
<tr>
<td>Obsessive-compulsive</td>
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Data analysis

Bivariate associations among target conditions were computed as tetrachoric correlations, which is the standard ap-
proach for factor-analytic studies of diagnoses and other dichotomous variables. Alternative classifications were compared using confirmatory factor analysis. First, we examined the fit of the 7-factor model, in which disorders were grouped according to the DSM-IV. Next, we tested the internalizing-externalizing model. Variables were assigned to factors based on findings of prior investigations. Conditions that had not been studied within this organization (manic episode and psychosis) were allowed to load on both dimensions. We also evaluated the hypothesized internalizing-externalizing thought-disorder model, with the latter dimension defined by psychosis, manic episode, and cluster A PDs.

Next, we examined modifications to these basic models as outlined in the first section of this article. The basic models assumed that the previously identified PD factors24 mapped onto the Axis I dimensions.6,20 To test this assumption, we first split the externalizing spectrum into Axis I and Axis II components and compared fit of the resulting organization with the original model. We then did the same with the internalizing spectrum. We were not able to split the thought disorder cluster because there were too few markers to define its Axis I component. Finally, we examined the structure within the internalizing spectrum by moving fear disorders (panic disorder, social anxiety, specific phobia, and obsessive-compulsive disorder) to a separate factor.

The models were analyzed with commercial software (Mplus version 5).35 In comparing these models, we considered 7 fit indices: the χ² goodness-of-fit statistic, the comparative fit index (CFI), the Tucker-Lewis index (TLI), the root-mean-square error of approximation (RMSEA), the Akaike information criterion (AIC), the Bayesian information criterion (BIC), and the sample-size adjusted BIC (ABIC).36-38 Although there are no strict criteria for evaluating these fit indices, conventional guidelines40 suggest values representing better fit.39,40 Conventional guidelines40 suggest that the CFI and TLI of 0.90 or more indicates adequate fit; RMSEA of 0.08 or lower indicates adequate fit and 0.06 or lower indicates excellent fit. There are no absolute cutoffs on the AIC, BIC, and ABIC, but these indices can be used to compare models, with lower values representing better fit.39-40 Conventional guidelines40 suggest that a difference of less than 6 is small, 6 to 10 is substantial, and more than 10 is very substantial.

RESULTS

BIVARIATE ASSOCIATIONS AMONG TARGET CONDITIONS

Tetrachoric correlations (Table 2) revealed strong associations among SUDs, antisocial traits, and conduct problems, with correlations ranging from 0.42 to 0.64. This pattern implies the presence of the externalizing spectrum in our data. Other cluster B syndromes and paranoid traits also correlated strongly with antisocial conditions and with each other (range, 0.35-0.62). However, their associations with SUDs were much weaker. Hence, it is unclear whether all these conditions define a single externalizing spectrum or the structure is more complex.

Correlations among mood, anxiety, and somatoform disorders were not as strong, although several were substantial (9 coefficients were >0.30). Of note, somatoform conditions correlated appreciably with each other (range, 0.27-0.36), but showed only weak associations with mood and anxiety disorders (all r values ≤0.20). This pattern may indicate a somatoform cluster that is distinct from the internalizing spectrum. In contrast, dependent and borderline traits had many notable links with mood and anxiety disorders.

Psychosis showed a close connection with schizotypal traits and was substantially associated with other cluster A conditions, which suggests the existence of a coherent thought disorder spectrum. However, the strongest correlate of psychosis was mania. Moreover, the 2 variables correlated more highly with each other than mania did with major depression (0.60 vs 0.30). This pattern indicates that these variables should be placed on the same factor.

COMPARISON OF BASIC MODELS

First, we examined a 7-factor model based on the DSM-IV. The factors were somatoform, anxiety, mood, psychotic, eating, substance use, and personality. The conditions were assigned to factors according to their placement into DSM-IV classes. Confirmatory factor analysis indicated that this organization fit the data poorly. The CFI and TLI were not acceptable, and this model was the worst on all fit indices (Table 3).

Next, we considered an internalizing-externalizing model, which was specified according to prior research.6,17,21,24,25 The internalizing spectrum included somatoform and anxiety disorders, major depressive episode, eating disorder, and cluster A and cluster C traits. The externalizing spectrum was composed of SUDs and cluster B traits. Borderline and paranoid traits were allowed to load on both dimensions because they did so in previous studies.22-24 To our knowledge, manic episode and psychosis have not been investigated within this framework, and we therefore allowed them to cross-load rather than making assumptions about their placement. This model performed better than the DSM-IV organization on all fit indices, although the CFI and TLI did not reach the acceptable level. The 2 dimensions correlated only moderately (r = 0.29). All factor loadings were larger than 0.30, which indicates good placement of variables in the model,41 with 2 exceptions. First, manic episode and psychosis had very weak loadings on the externalizing factor (0.12 each), in contrast to their appreciable loadings on the internalizing factor (0.39 and 0.34, respectively). Evidently, these conditions can be placed in the internalizing cluster and their externalizing loadings can be constrained to zero. Second, all somatoform disorders had low loadings (range, 0.21-0.29), which indicates that they did not fit clearly in the 2-spectrum model. To capture these conditions, we had to specify an additional somatoform factor.

The resulting 3-factor model was identical to the internalizing-externalizing organization except that somatoform disorders went on the third dimension rather than the internalizing factor. In addition, manic episode and psychosis were allowed to load only on the internalizing dimension. These changes resulted in significantly better fit, as indicated by the AIC, BIC, and ABIC. The CFI and TLI improved but remained just below the threshold for acceptable fit. All somatoform disorders were well captured by the model, with their factor loadings ranging from 0.49 to 0.61. The correlation between the internalizing and somatoform factors was modest (r = 0.43),
which is further evidence of a separate somatoform spectrum. Additional refinements were necessary given the marginal fit of this organization.

Next, we specified a 4-factor model by splitting psychosis, manic episode, and cluster A traits from the internalizing group and placing them on the thought disorder dimension, as hypothesized. Paranoid traits were allowed to cross-load on internalizing and externalizing factors, as they did in prior research. This model showed much better fit on all indices. The TLI and CFI were now in the adequate range, and the RMSEA was excellent. All variables loaded well.

The 4-factor model differed from the 3-factor model only in that manic episode, psychosis, and cluster A traits were moved to the thought disorder dimension; paranoid traits were allowed to cross-load on internalizing and externalizing factors. The 5-factor model split externalizing conditions of the 4-factor organization into externalizing and antagonism factors (Figure). The 6-factor A model replicated the last organization but separated Axis I internalizing conditions (major depressive episode, panic disorder, social anxiety, specific phobia, and obsessive-compulsive disorder) from the internalizing factor. The 6-factor B model is a modification of the 5-factor organization in which fear disorders (panic disorder, social anxiety, specific phobia, and obsessive-compulsive traits) and Axis II internalizing traits (paranoid, dependent, and obsessive-compulsive traits) from the internalizing factor.
Next, we modified the resulting organization by splitting the internalizing spectrum into Axis I internalizing (major depressive episode, eating disorder, and anxiety disorders) and Axis II internalizing (paranoid, borderline, dependent, and obsessive-compulsive traits). This 6-factor model (6-factor A in Table 3) fit the data worse than the 5-dimension organization, as indicated by the BIC and ABIC. Thus, the slight improvement in absolute fit (ie, the CFI, TLI, and RMSEA) was not sufficient to justify the model's increased complexity. Moreover, the correlation between Axis I internalizing and Axis II internalizing factors was 0.96, indicating that they are essentially the same dimension. Hence, this model was rejected in favor of the 5 spectra.

We also examined the possibility of separating fear disorders from other internalizing conditions. This 6-factor organization (6-factor B) fit the data similarly to the 6-factor A model. It was slightly better than the 5-factor organization on the AIC, but this difference was very small. In contrast, the BIC and ABIC clearly indicated that the 5-factor model is superior. The fear and internalizing factors correlated 0.93, which suggests that they should be combined. Thus, the 5-spectrum organization was more parsimonious and emerged as the best classification scheme in our analyses.

This study extended research on the quantitative nosology in several ways. First, it confirmed the internalizing, externalizing, and thought disorder spectra in a clinical population. These clusters have been observed in community and inpatient samples, and we now have replicated them in outpatients. Second, we examined Axis I and Axis II disorders jointly and found that, although most personality pathology fits into the 3 spectra discussed herein, some conditions (cluster B and paranoid PD) reflect a distinct antagonism dimension. Third, our analyses included several Axis I conditions that were not studied previously in the quantitative framework, namely, mania and somatoform disorders. The former was linked to the thought disorder spectrum, whereas the latter formed a separate cluster. Overall, this investigation represents a significant advance in classification research; it is the most comprehensive study to date and was performed in a large, carefully diagnosed outpatient sample.

Our hypotheses were generally supported. As predicted, we found that the DSM-IV organization fits the data poorly. It had the worst fit of the models considered, despite being the most elaborate. The internalizing, externalizing, and thought disorder spectra emerged as hypothesized. We also observed 2 additional dimensions: antagonism and somatoform. These spectra are defined by high negative affect (internalizing), extreme trait disinhibition (externalizing), odd/eccentric cognition and behavior (thought disorder), callous antipathy (antagonism), and maladaptive responses to somatic symptoms (somatoform).42,43 We replicated the 3 personality pathology dimensions reported by O'Connor.24 His model
did not include somatoform and externalizing spectra, which are defined primarily by Axis I conditions and could not have been identified in analyses restricted to PDs. O’Connor’s dimensions mapped onto the internalizing and thought disorder spectra as expected, whereas the antagonism dimension was unique to Axis II.

The present investigation builds on Markon’s analyses of Axis I and Axis II symptoms. In addition to the internalizing, externalizing, and thought disorder spectra observed by Markon, we found somatoform and antagonism dimensions. We were able to detect these additional spectra because we had better coverage of somatoform and cluster B conditions. We did not observe Markon’s pathological introversion factor, likely because he evaluated several relevant symptoms, whereas we analyzed diagnoses, which provided few clear markers of that dimension.

Overall, our syndrome-based analysis confirmed the major symptom dimensions. The 2 approaches are complementary. Syndrome-based analyses directly inform a diagnostic system but are tied to diagnoses specified within it. A symptom-based approach is not bound by a particular system and can address heterogeneity within disorders. Convergence between these approaches provides important evidence of the spectra’s fidelity.

A distinct fear cluster within the internalizing spectrum is well documented, although not all studies find evidence of the spectra’s fidelity. We analyzed diagnoses, which provided few clear markers of that dimension. Overall, our syndrome-based analysis confirmed the major symptom dimensions. The 2 approaches are complementary. Syndrome-based analyses directly inform a diagnostic system but are tied to diagnoses specified within it. A symptom-based approach is not bound by a particular system and can address heterogeneity within disorders. Convergence between these approaches provides important evidence of the spectra’s fidelity.

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Mania had only a moderate association with major depression. Although lifetime depression was prevalent in patients with lifetime mania (90.6%), depressive episodes were similarly common in several internalizing disorders (e.g., posttraumatic stress disorder, dependent traits). In addition, the prevalence of mania was not elevated in patients with lifetime depression (4.1%) but was high in the schizotypal (10.7%) and psychosis (19.1%) groups. These findings are consistent with proposals to dissolve the mood disorders class and research suggesting that bipolar disorder differs from unipolar depression on many validators.45-46 Mania may fit better on the thought disorder spectrum. Indeed, mania shares features with these conditions, including frank psychosis (observed in 47% of our patients with bipolar I disorder), disorganized thought, tangential speech, and bizarre behavior. However, mania does not show the negative symptoms common in schizoid PD and some forms of schizophrenia. Hence, relations within the spectrum are complex and require further study. We could not investigate them here because we lacked data on specific psychotic syndromes due to hierarchical rules of the DSM-IV. Different assessment strategies can overcome this limitation.20

The emerging quantitative classification ultimately may provide a more useful guide to the field than the DSM-IV. Indeed, factor-analytically derived spectra appear to reflect core genetic vulnerabilities. Twin studies52-53 have reported that shared genetic factors underlie each of the 5 dimensions observed in the present investigation. Thus, an explicit focus on these spectra can aid research on genetic etiologies. In fact, molecular genetic studies are beginning to identify specific genes contributing to the 3 established spectra.54-56 We hope that our findings will stimulate parallel work on the somatoform and antagonism dimensions. Research on other diagnostic validators, such as neurobiological underpinnings and treatment response, produced preliminary support for the usefulness of internalizing, externalizing, and thought disorder clusters.27-29 More such research is needed on all 5 spectra.

Strengths of the study include the large sample size and diagnostic ascertainment by clinicians who used state-of-the-art semistructured interviews. Nevertheless, these findings need to be considered against the limitations. Although our approach was firmly grounded in prior studies, we examined many disorders not considered previously, and our analyses were, in part, exploratory. Indeed, 2 of the identified dimensions are novel and require replication. However, the current investigation was limited to 25 conditions even though it was much broader than prior studies. Future research needs to examine many more disorders to explicate a comprehensive quantitative classification system. In addition, we had to exclude avoidant PD for analytic reasons, but given its high overlap with social phobia, avoidant PD clearly belongs on the internalizing spectrum. Factor-analytic studies, including ours, analyze nonhierarchical syndromes. Nosologists will need to refine identified organizations and add hierarchical rules whenever a syndrome may be secondary to other conditions. Finally, the present study was conducted in a single clinical practice in which patients were predominantly white and female and had health insurance. This may have affected the results, and the study should be replicated in clinical samples with different demographic characteristics and presenting concerns.

In conclusion, this study is the most comprehensive investigation of the quantitative nosology to date, and thus it was able to identify novel somatoform and antagonism spectra. We also confirmed the internalizing, externalizing, and thought disorder spectra in an outpatient population, providing crucial evidence of their validity in clinical settings. These 3 dimensions are gaining recognition and have been included in a proposed meta-structure for DSM-5.13 Current findings underscore the need to reorganize the diagnostic system, especially since the DSM model fit the data so poorly. Our results are consistent with proposals to relocate PDs to Axis I in DSM-533,33 because we observed close links between PDs and clinical disorders: cluster A with psychotic disorders, cluster C and borderline with depressive and anxiety disorders, and antisocial disorder with SUDs. However, we found that cluster B PDs define a distinct group. An antagonism class may need to be added.
to Axis I or an antagonism trait domain included on Axis II. Our findings also indicate that unipolar depression clusters with anxiety disorders rather than with bipolar disorders, which reinforces the calls to dissolve the mood disorders class.11,14 Some of the present findings require replication, and other disorders need to be incorporated into this system. Ultimately, these advances are expected to enhance the validity and practical usefulness of psychiatric diagnosis.

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