AXIS II COMORBIDITY AND ITS EFFECT ON AXIS I DIAGNOSIS AND MANAGEMENT

Elena Raluca Barbu\textsuperscript{1}, Andreea Custureac-Popescu\textsuperscript{2}, Dan Prelipceanu\textsuperscript{3}

Abstract: Ongoing research demonstrates a striking tendency for personality disorders and mental illness to co-occur; almost all Axis I categories being associated with maladaptive personality traits/criteria across the three personality disorder clusters. The high comorbidity rates between the two axes can be explained by models of association, the structure of personality and even common genetic vulnerabilities. As these links are being identified, the distinction between Axis I and Axis II traditional diagnostic formulations are becoming increasingly blurred, indicating the need for new nosological systems. We present a brief review on the implications of Axis II comorbidity in diagnosis, treatment and prognosis of mental disorders.

Key words: personality disorders, mental illness, associations, treatment

INTRODUCTION

Many patients seen in a clinical psychiatric setting often present with more than one problem. Aside from mental illness (clinical disorder), these problems may include personality disorders, substance misuse, as well as social difficulties and general medical conditions. The multi-axial classification system was first introduced in 1980 by DSM III and placed personality disorders (Axis II) on a different axis from other clinical disorders (Axis I), generating a wealth of research on the co-occurrence of mental illness and personality disorders. The comorbidity and relationships between Axis I psychiatric disorders and Axis II personality disorders varies within each disorder and across the personality disorders. The clinical significance of Axis I–Axis II disorder associations lies in the fact that the management of mental illness is more complex in the presence of personality disorder (1).

COMORBIDITY, PERSONALITY AND MODELS OF ASSOCIATION

The term comorbidity was coined by Feinstein (1970) and introduced in the medical literature to denote the presence of “any distinct additional clinical entity that has existed or may occur during the clinical course of a patient who has the index disorder under study” simultaneously with the primary disease (2).

Numerous studies have documented extensive comorbidity among psychiatric disorders and raise fundamental questions about psychopathology and the classification system, concern being expressed about the overlap in diagnostic categories, the lack of clear cut separation between mental illness and personality disorders and the difficulty of diagnosing personality disorders in patients that present with an acute episode of clinical disorder (3). Results from clinical and population studies indicate that comorbidity between disorders is actually the rule rather than the exception and diagnoses co-occur more frequently than it would be expected by chance (4, 5). This findings raise questions about the mechanisms resulting in these associations and their importance for the management of the disorder in question. Several models of association have been proposed. Klorman (1990) suggested a primary-secondary distinction approach to comorbidity: chronological, causal or symptomatic (6). Krueger & Markon (2006) propose the hierarchically organized liability spectrum model of comorbidity, in which comorbidity is understood as a function of underlying vulnerability for psychopathology. The model suggests that specific mental disorders are diverse expressions of underlying vulnerabilities and that psychopathology is rather continuous than categorical. The authors developed the following models to explain comorbidity: bivariate models that consider only two disorders occurring simultaneously, multiformity models (the expression of vulnerability is heterogeneous), causation models (i.e., one disorder vulnerability directly causes the development of a second disorder or reciprocal causation in which both disorders may cause one another), an independence model (disorders have independent vulnerabilities), and spurious association models (external factors create the association) (7).

A variety of characteristics could form the basis for distinguishing between the two diagnostic categories: stability, age of onset, treatment response, insight, comorbidity and symptom specificity, and etiology, but none of them have been proven to set a clear distinction between the two axis diagnosis. The most promising general direction for research would therefore focus on understanding how and why the two domains are so interconnected and the answer to this question could be provided by the structure of personality (8). The Five Factor Model (or Big Five) appears to represent a compelling model for organizing normal and abnormal personality variation, including the variation captured by the personality disorders categories described in the DSM–IV–TR (9). Comorbidity among common mental disorders makes sense when thought of in terms of the personalonomic underpinnings of these disorders. Krueger et al. (1998) demonstrated that unipolar mood and anxiety disorders were indicators of a latent internalizing propensity (negative emotionality or neuroticism with...
two subspectrums: distress and fear), and substance dependence and antisocial behavior disorders were indicators of a latent externalizing propensity (negative emotionality and disinhibition) (10). Kendler et al. (2003) studied the genetic and environmental underlying comorbidity among seven syndromes (major depression, generalized anxiety disorder, phobia, alcohol dependence, other drug abuse or dependence, adult antisocial behavior, and conduct disorder) that delineate the internalizing and externalizing spectra, the results strongly suggesting that genetic factors are responsible for this pattern of comorbidity (11).

In comparison to other branches of medicine where diseases are relatively well delineated, psychiatry deals mostly with disorders, that is to say behavioral and psychological syndromes that are deviant from some standard of normality. Mental illnesses/disorders are polygenetic, multifactorial, and developmentally complex (12). Clinical assessment should lead to individualized diagnostic formulation, involving consideration for treatment and prognosis, as comorbidity results in more functional impairment than the cumulated effects of the disorder itself (13).

Research has suggested that between 66% and 97% of patients with personality disorders also experience mental illness, and that between 18% and 81% of those with mental illness also have a personality disorder (14).

In the following sections we will discuss the different associations that have been shown to exist between different personality disorders and mental illness.

MOOD DISORDERS AND COMORBID PERSONALITY DISORDERS

Mood disorders, both unipolar and bipolar, are recurrent and frequently refractory to treatment and the presence of maladaptive personality features in these patients is often seen as a poor prognostic indicator, being related to increased suicide risk, worse therapeutic response, adherence problems, increased frequency of mixed and depressive features (15, 16). There is ongoing debate regarding the way we conceptualize personality traits as contributing or being tightly integrated in the clinical presentation of affective disorders.

The rate of comorbid personality disorders in patients with depression varies between 43% and 64%, suggesting that comorbid personality pathology, however defined, is common in depressed patients and potentially important in management consideration of each case. The most common personality disorders appear to be avoidant, borderline and more variably, paranoid and obsessive-compulsive personality disorders (17, 18). The relationship between personality disorder and depression can be conceptualized in several ways, three or four concepts have been proposed by researchers: “the vulnerability or predisposition model” (the tendency of maladaptive personality traits to predispose an individual to develop depression); “the complication or “scar” model” (the development or exaggeration in personality traits as a complication of depression-especially chronic or early onset depression); “the spectrum or coaggregation model” (depression and some personality disorders overlap phenomenologically, as a result of common etiology and vulnerability); “the pathoplasty model” (the influence of personality disorders on the clinical presentation of depression, its course and its response to treatment) (19, 20). None of these models are mutually exclusive, and they only represent a conceptualization of the association between personality traits and depression. Kendler et al. used a twin sample registry to demonstrate the relationship between depression and neuroticism, reporting a strong association between the two that was largely mediated through genetic factors rather than as a causal pathway, neuroticism implying a high genetic risk for depression, low self-esteem and early onset anxiety disorders (21). Mulder et al. reported an increased rate of chronic depression in individuals with comorbid personality disorders (22). It is believed that many personality manifestations, such as some avoidant, borderline, dependent traits and neuroticism scores as well are actually features of depression. There is consistent evidence that when individuals are no longer depressed, maladaptive personality traits have lower rates and so have neuroticism scores (23). These findings suggest that depression and personality disorders are not simply comorbid or independent, but they rather commonly tend to be found together. The most soaring problem posed by this Axis II-Axis I association is the clinical importance of it, opinions differing on this subject. Newton-Howers and Tyrer (2006) conclude that comorbid personality disorder with depression was associated with a doubling of the risk of a poor outcome for depression compared with no personality disorder, with the side note that it was not possible to conclude that personality disorder in itself caused the poorer outcome in depression (16). On the other hand, Bieger et al. (2002) reported that comorbid personality disorder was unrelated to the course or outcome of depression, except for age of onset, number of suicide attempts, and quality of life, and Mulder (2002) reported that there was no overall effect on outcome from having a comorbid personality disorder in 183 outpatients (22, 24).

Bipolar disorder is a common psychiatric illness. Estimates suggest that bipolar disorder affects approximately 2% of the population, although estimates of the lifetime rate of bipolar spectrum disorder approach 5% (25). Conceptual models linking personality and bipolar disorder are relatively underdeveloped compared with models for major depressive disorder. The incidence of comorbid personality disorder ranges from 45% to 65%, with borderline personality as the most prevalent, followed by histrionic personality disorder (26). To avoid misdiagnosis and overlap, given the notion of bipolar spectrum, the presence of a personality disorder in a bipolar patient should be assessed only during the euthymic phase. Patients with bipolar disorder and a diagnosis of personality disorder are more likely to be hospitalized, require more time to achieve symptom stabilization, have more chronic impairments in occupational and social functioning, are less compliant to medication, have greater levels of suicidality and utilize more psychiatric services than patients with bipolar disorder alone (27). The presence of a personality disorder or maladaptive personality traits (cluster B, especially borderline personality disorder) was associated with higher rates of alcohol/drug abuse disorder, anxiety disorders and are a lower rate of full functional recovery in bipolar patients (28, 29). Bipolar patients who associate a personality disorder tend to respond less well to
pharmacotherapy and it takes a longer time to achieve stabilization and there are larger number of relapses (30, 31). Furthermore, comorbid bipolar patients are more likely to have suicidal ideation than single diagnosis patients (32).

**ANXIETY DISORDERS AND COMORBID PERSONALITY DISORDERS**

Personality traits and most anxiety disorders are strongly related. Personality traits may relate to anxiety disorders as predisposing factors, as consequences, as results of common etiologies, and as pathophysiological factors (33). Regarding personality disorder traits, antisocial, borderline, dependent, depressive, histrionic, passive-aggressive, and schizotypal personality traits present in adolescence and early adulthood (between ages 14 and 22) were associated with increased risk of having an anxiety disorder by middle adulthood (mean age of 33), controlling for baseline anxiety disorders (34). Personality traits such as high neuroticism, low extraversion, and personality disorder traits (particularly those from cluster C) are at least markers of risk for certain anxiety disorders (35). The existence of comorbid personality disorders predict worse outcome in patients with anxiety disorders. For example, in a treatment study of patients with panic disorder, comorbid personality disorders, particularly avoidant, were associated with a delayed response to treatment (36). Patients with generalized anxiety disorder and comorbid avoidant or dependent personality disorders had a lower probability of remission at 5 years than those without personality disorders and socially phobic patients with avoidant personality disorder were less likely to remit from social phobia (37). Obsessive-compulsive disorder associated with substantial schizotypal personality traits (for example, unusual perceptual experience) seems to have poorer response to treatment (38). The presence of comorbid paranoid or borderline personality disorder predicted suicide attempts, and avoidant personality disorder predicted suicidal ideation (39). Genetic factors may help explain why personality traits are so strongly related to most anxiety disorders and there is evidence that the same genes that influence neuroticism also influence risk for generalized anxiety disorder, for example (40).

**SUBSTANCE USE DISORDERS AND COMORBID PERSONALITY DISORDERS**

Personality disorders, in particular, are considered to be an important contributing and/or predisposing factor in the pathogenesis, clinical course and treatment outcome of substance use disorders. Antisocial personality disorder has the strongest and most specific association with substance abuse/dependence. Although the association might reflect overlap in diagnostic criteria (i.e. drug use leading to antisocial behavior), it can still be detected when drug-related behavior is excluded from the diagnosis of antisocial personality disorder (41). Early antisocial behavior, in the form of conduct disorder, is a common antecedent of substance dependence; genetic studies suggesting etiological links between the two disorders (42).

Almost the whole spectrum of personality disorders can be encountered in alcohol dependence, such as the antisocial, borderline, dependent, avoidant, paranoid. The prevalence of personality disorders in alcoholism ranges from as low as 22.40% to as high as 58.78% (43). Using the data from the NESARC epidemiological study of over 40,000 individuals and applying a revised method of diagnosing personality disorders, researchers found that the highest comorbidity rates for lifetime alcohol dependence were observed among those with antisocial (52.09%), histrionic (49.79%), and borderline (47.41%) personality disorders. Highest rates of comorbidity with drug dependence occurred among those with histrionic (29.72%), dependent (27.34%), and antisocial (26.65%) personality disorders. Finally, odds ratios are high for almost all personality disorders and nicotine dependence (44).

**SCHIZOPHRENIA AND COMORBID PERSONALITY DISORDERS**

Kety et al. revealed a schizophrenia spectrum term for all disorders transmitted genetically to a degree together with schizophrenia (45). The disorder possibly varies in a broad, continuous range from subthreshold forms to severe clinical forms, in which schizophrenia represents the range’s endpoint. Schizotypal personality disorder was included in this spectrum with strong evidence resulting from various family studies, and with moderately strong evidence paranoid and schizoid also (46). Avoidant personality disorder was also proposed for inclusion in the spectrum (47). In a study of premorbid personality disorders in schizophrenic patients with and without substance use disorders, the most common premorbid personality disorders in patients without comorbidity were avoidant (35%), paranoid (17.5%) and obsessive–compulsive (15%), whereas in the group with substance abuse comorbidity, the most common PDs were borderline (37.5%), antisocial (35%) and paranoid (22.5%) (48).

**SOME CONSIDERATIONS**

Eating disorders are multidetermined psychiatric disorders that may also be influenced by personality pathology. Anorexia nervosa, restrictive type is found to be in association with obsessive compulsive personality disorder, this personality pathology occurring with a 22% reta of prevalence. Borderline personality disorder has a prevalence rate of 25% in anorexia nervosa, binge-eating purging type, borderline being also the most common personality disorder in bulimia nervosa (28%) (49).

Attention deficit hyperactivity disorder portends risk for adult personality disorders, but the risk is not uniform across disorders, nor is it uniformly related to child or adult diagnostic status (50).

Clinical or mental disorders are recorded on the first of the five DSM axes used to classify psychiatric pathology, and personality disorders are described on the second of those five axes. Shall we continue to separate mental disorders into these two categories or is it time to reconstruct this arrangement? Current research on the association between personality and psychopathology indicates rather a closer connection between these two diagnostic categories than it is implied by their separation on the two axes. One way to understand this connection is from the point of view of general personality functioning and individual differences, providing a framework that is very useful to understanding psychopathology in general.
Furthermore, this close connection is backed up by genetic studies. A recent genome-wide association study of borderline personality disorder reveals genetic overlap with bipolar disorder, major depression and schizophrenia, just to give one example (51).

CONCLUSIONS
There seems to be complex associations and a great deal of co-occurrence between Axis I clinical disorders and Axis II personality disorders, relationships that vary within each disorder and across personality disorders. This situation appears to be the rule rather than the exception, raising questions about boundaries between disorders, the categorical method of classification and the overall clinical model of assessing and managing psychiatric pathology. Several models of association have been proposed in order to conceptualize the intricate relationship between clinical and personality disorders. The environmental and genetic underpinnings of psychopathology have contributed to explaining and enhancing these observations. It seems it is high time to acknowledge that the boundaries between disorders are not quite as clear as previously thought.

REFERENCES


***

*Conflict of interest: none declared
Financial support: none declared*