



## Interaction effects in comorbid psychopathology

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### Abstract

**Purpose:** Comorbidity in psychopathology is the norm. Despite some initial evidence, few studies have examined if the presence of comorbid conditions changes the expression of the pathology, either through increased severity of the syndrome(s) or by expanding to symptoms beyond the syndrome(s) (i.e., symptom overextension). The following report provides an illustration of interactive effects and overextension in comorbid pathology.

**Method:** A large pool of patients from a university hospital were assessed using SCID-I/P interviews. Of these, 230 patients diagnosed with major depressive disorder, social phobia, or both were included in the study.

**Results:** Symptoms not belonging to either index condition (major depressive disorder or social phobia) reliably overextended in comorbid cases (odds ratios between 2.82 and 15.75).

**Conclusions:** Current research methodologies (e.g., structured interviews) do not allow for the examination of overextended symptoms. The authors make a call for future psychopathological research to search systematically for interactive effects by adopting more inclusive or flexible assessments.

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### 1. Introduction

The co-occurrence of multiple psychiatric disorders in an individual is a common phenomenon within psychopathology [1]. Diagnostic comorbidity is so prevalent that it may be the rule, not the exception [1]. These high rates of comorbidity have presented several challenges to the current conceptualization of mental disorders as discrete diagnostic entities, articulated in the *DSMs* and *ICDs*. If the disorders are indeed discrete, then their overlap far exceeds what would be expected by chance [1–3]. Although a portion of this overlap may be diagnostic “noise” or an artifact attributable to symptom overlap across diagnoses [4], substantial comorbidity exists even when eliminating overlapping symptoms [5,6]. Many researchers have argued that, instead of being noise, diagnostic overlap may be a meaningful “signal” which can inform models of psychopathology [7].

One view of diagnostic comorbidity, which has gained considerable research support, is that patterns of diagnostic comorbidity represent underlying dimensions or vulnerabilities among disorders. For example, the high level of overlap between depressive and anxiety disorders may reflect a common distress syndrome that is merely expressed in a variety of ways [8–11]. Indeed, several studies have suggested that diagnostic overlap reflects underlying genetic vulnerabilities or personality patterns that manifest in different ways leading to specific disorders [12–16]. These studies reflect a latent variable model of comorbidity.

Another explanation of comorbidity has focused on the interactions between symptoms within and across disorders [17]. Under models like this, comorbidity represents the relationship between individual symptoms that may cause—or at least influence—the expression of each other. For example, insomnia may lead to fatigue (a causal link within a syndrome), which then can deplete cognitive resources, leading to increased anxiety (a causal link across syndromes). Thus, this model accounts for comorbidity through an inter-related network of causal connections between symptoms and does not refer to latent constructs or vulnerabilities.

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One potential limitation of the above models is that they are based, at least in part, upon discrete diagnostic syndromes as they are currently defined in the *DSM* and *ICD*. Although no model holds any special commitment to *DSM* or *ICD* definitions of disorders *per se*, they are limited to simple additions of symptoms from syndromes when describing comorbid presentations. Neither approach specifically postulates any changes to the diagnostic syndromes or their presentation when comorbidity is present.

In contrast, a growing body of literature has found that the presence of a comorbid disorder changes the presentation of the index condition. There are two ways this idea could be expressed. First, a comorbid disorder tends to lead to the presence of additional symptoms [18] or greater overall severity of the symptoms [19] within the syndrome. In other words, the presence of an additional disorder increases the severity of the first condition. This relationship has been long recognized in the literature. However, a second possibility is that the presence of a second disorder could alter the presentation of one or both conditions beyond the boundaries of the original syndrome(s) [20]. In other words, the comorbid expression of two disorders may include symptoms that are not part of either single disorder. For example, the combination of Major Depressive Disorder and Generalized Anxiety Disorder may result in symptoms, like interpersonal submissiveness, that reliably emerge as what Keeley and Blashfield [20] term “overextensions.” In other words, the combination of disorders A and B may not result in an additive concept AB, but rather in a new concept C that includes its own unique features [21]. Consistent with this hypothesis, Keeley and Blashfield [20] found that mental health professionals often included such overextensions in their descriptions of comorbid symptom patterns. While it is reasonable to assume that clinicians’ conceptualizations would be based upon the pathology they have encountered in their work, other influences like education or theoretical orientation may also influence the way they see disorders. It remains to be tested if overextensions would emerge from observations of clinical patients based on symptoms derived from formal diagnostic structured interviews.

If interactive effects exist, they would hold a number of implications for research and clinical practice. First, the field may be systematically ignoring relevant symptomatology. Standard assessment methods, particularly standardized interviews, may miss these features. Clinically, these symptoms may be untreated, and could account for variance in treatment response and recovery. In research, the usual practice of selecting “clean” samples of individuals meeting a single diagnosis may drastically misrepresent common expressions of psychopathology, and research on comorbidity *per se* may be muddied by “noise” symptoms that actually represent systematic effects. Identifying overextended symptoms may guide researchers to investigate heretofore unconsidered common causal pathways for psychopathology.

These interactive effects and potential overextended symptoms have been rarely investigated. One reason for the paucity of such research is that although diagnostic comor-

bidity is quite common, comorbidity of specific pairs of disorders is rarer. Therefore, very large samples are required to generate enough individuals with the same comorbid conditions to accurately search for systematic patterns of symptoms among them. In the current investigation we examine comorbid symptom patterns using a large psychiatric population sufficiently powered to produce reliable estimates of such patterning (observed power = 0.959) [22]. It should be noted that the specific pair of disorders was not considered any more theoretically meaningful than other diagnostic pairings; rather, our purpose was simply to investigate one example of possible interactive effects in comorbid pathology.

## 2. Method

### 2.1. Participants

Participants were drawn from a database of 2325 patients who had been referred for psychological/psychodiagnostic assessment and evaluation at a tertiary care, university affiliated psychiatric hospital. Parts of these data have been reported in other studies with a different focus [23–25]. Participants were included in the current study if they met *DSM-IV* diagnostic criteria for major depressive disorder (MDD), social phobia (SP), or both. Importantly, there were no exclusionary criteria, so patients could also meet diagnostic requirements for other disorders. This resulted in a total of 230 patients. One-hundred nineteen participants met criteria for MDD but not SP, 75 for SP but not MDD, and 36 for both MDD and SP. These two disorders were selected because they represented the highest frequency of comorbidity between any two diagnoses in the larger sample, and a high rate of comorbidity in the population generally [1]. Participants were 57.8% female, with an average age of 34.28 years ( $SD = 13.18$ ). All procedures were approved by institutional IRBs and participants provided voluntary consent.

### 2.2. Materials and procedure

As part of routine clinical assessment, all patients referred to the Psychological Assessment Service were administered the *Structured Interview for DSM-IV Axis I Disorders - Patient Edition* (SCID-I/P) [26]. The SCID-I/P was administered by registered clinical psychologists or clinical psychology graduate students (either interns or practicum students) or master’s level clinical psychologists (psychometrists). All staff and students had been formally trained in the administration and scoring of the SCID-I/P.

### 2.3. Analysis

To examine if comorbid presentations result in systematic overextensions, we calculated the frequency with which participants met criteria for each symptom on the SCID-I/P (not just those relevant for their diagnosed disorder) for each diagnostic group (MDD, SP, comorbid). We then calculated odds ratios based upon those frequencies to examine if

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