



Published in final edited form as:

Psychiatry Res. 2015 January 30; 225(0): 179–186. doi:10.1016/j.psychres.2014.11.017.

Is a Gin and Tonic More Like Gin or Tonic? A Comparison of Comorbid and Non-Comorbid Anxiety Disorder Diagnostic Pairs

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Abstract

Despite findings indicating that anxiety disorders are more likely to co-occur with each other than occur in isolation, little research has explored precise areas of overlap and differentiation among comorbid pairs of anxiety disorders. Furthermore, many studies comparing phenomena across anxiety disorders define comparison groups based on principal diagnoses, with lesser regard for comorbid diagnoses, raising the question as to whether this is a valid approach to analyzing comparisons. To better understand the extent to which comparisons by principal diagnoses are valid, the current study investigated whether comorbid hierarchically opposing diagnostic pairs showed similarities and differences from their non-comorbid, or “pure,” counterparts on measures of clinician-rated functioning, specific symptoms, vulnerability factors, and demographic characteristics. The study included a total of 353 participants with diagnoses of either Panic Disorder only, Social Phobia only, Generalized Anxiety Disorder only, or some comorbid pair of the three. Consistent with hypotheses, results demonstrated that hierarchically opposing diagnostic pairs showed more overlap than differentiation with each other and with non-comorbid counterparts on measures of a given specific non-comorbid diagnosis, indicating that defining comparisons by principal diagnoses may be invalid and misleading. The implications regarding the nosological structure of the DSM and research practice will be discussed.

Keywords

anxiety disorders; comorbidity; comorbid pairs; principal diagnoses; additional diagnoses

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1. Introduction

The disproportionately high rates of co-occurrence and overlap among psychiatric disorders have been a long-standing issue with the nosological system of the DSM (Widiger and Samuel, 2005; Keeley et al., 2013). In fact, epidemiological research has indicated that at least half of those with a psychiatric diagnosis are likely to meet criteria for one or more comorbid diagnoses (Kessler et al., 2005). According to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, text revision (DSM-IV-TR), and 5th edition (DSM-V), if patients present with more than one Axis I diagnoses, the principal diagnosis or reason for visit should be listed as a principal diagnosis, with all subsequent diagnoses listed beneath it accordingly as comorbid diagnoses (American Psychiatric Association [APA], 2000, 2013). Therefore, as Keeley and colleagues (2013) have described, the current and former DSM system uses an additive model to conceptualize comorbidity among disorders (e.g., “Disorder A + Disorder B = Disorder AB” [p. 17]). For example, an individual with a principal diagnosis of Panic Disorder (PD) who is subsequently diagnosed with Social Phobia (SP) would ultimately receive a diagnosis of (PD+SP) whereas an individual with a principal diagnosis of SP who is subsequently diagnosed with an additional diagnosis of PD would ultimately receive a diagnosis of (SP+PD).

Although the DSM clearly defines the principal diagnosis as the “reason for visit,” it also acknowledges the difficulty of determining the principal diagnosis in practice, especially when clients present with more than one reason for visit, equally in need of attention (APA, 2000, 2013). However, as the DSM does not explicitly state how clinicians should address this predicament, clinicians in such a case may feel compelled to use alternative definitions of principal diagnosis (e.g., most severe diagnosis, diagnosis responsible for symptoms, etc.), possibly posing challenges to diagnostic reliability.

Anxiety disorders often present with high rates of overlap and comorbidity among each other (Brown and Barlow, 1992; Kroenke et al., 2007). For instance, Kroenke et al. (2007) found that, out of 199 patients with DSM-IV diagnoses of either generalized anxiety disorder (GAD), PD, or SP across 15 U.S. primary care clinics, 61.3% had one or more additional (i.e., non-principal) anxiety disorder diagnoses. Despite the apparent evidence that comorbidity within anxiety disorders is more common than anxiety disorders occurring in isolation, the nature of the relationships among comorbid anxiety diagnoses remains unclear. That is, less research has explored precise areas of overlap and differentiation within comorbid anxiety disorders, factors which might help us better understand the etiology, maintenance, treatment, and prognosis of anxiety disorders.

Furthermore, in revisiting our previous example of the individual with a principal diagnosis of PD and additional/comorbid diagnosis of SP [i.e., (PD+SP)], it stands to reason that this individual would exhibit a high degree of overlap with an individual who has a principal diagnosis of SP and additional comorbid diagnosis of PD [i.e., (PD+SP) \approx (SP+PD)]. Yet, most research comparing phenomena across diagnoses has focused predominantly on differences across principal diagnoses, with lesser regard for additional, non-principal diagnoses. Thus, these two combinations [i.e., (PD+SP) and (SP+PD)] are often examined as separate categories (principal PD vs. principal SP). Barrera and Norton (2009), for

example, conducted an analysis of the potential impact of anxiety diagnoses on subjective quality of life using a DSM-IV diagnosed sample of patients with PD, SP, or GAD seeking outpatient treatment. Although Barrera and Norton reported that “the majority of the sample (65%) had comorbid anxiety” (p. 1087), their primary analyses disregarded additional comorbid anxiety diagnoses and directly compared indices of quality of life across principal diagnoses. Lochner et al. (2003) also conducted a study comparing objective quality of life in DSM-IV principal diagnoses of OCD, SP, and PD, irrespective of comorbid conditions, and found a similar degree of overall functional impairment across groups, although some differences across diagnoses emerged in specific domains of quality of life impairment. Although Lochner et al. (2003) did not report rates of non-principal diagnoses within their sample, the authors indicated that “patients were classified according to their main psychiatric symptoms as having OCD, PD, or SAD [social anxiety disorder], irrespective of secondary comorbid conditions” (p. 256, clarification ours).

Studies have also examined the extent to which patients with differing principal anxiety disorder diagnoses differ on predispositional vulnerability factor variables. For example, Intolerance of Uncertainty (IU), a trait-like dispositional variable, was originally theorized to be specifically related to GAD (Boelen and Reijntjes, 2009; Mahoney and McEvoy, 2012). However, research on the specificity of IU to GAD has yielded mixed findings (Starcevic and Berle, 2006). For instance, Mahoney and McEvoy (2012) found high levels of IU in SP, but only included participants with principal diagnoses of SP despite high (77%) rates of comorbidity. Another study indicated that IU successfully discriminated between GAD and PD, but only used pure diagnoses of GAD and PD (Dugas et al., 2005). Therefore, the extent to which comorbidity may have contributed to these findings is unclear. Other studies using dimensional measures of anxiety features, rather than formal diagnoses, have indicated that IU is related to a variety of anxiety characteristics (e.g., fear of negative evaluation, anxiety sensitivity, OCD features, worry; Boelen and Reijntjes, 2009; Carleton et al., 2010). Thus, including comorbidity may provide a more accurate picture of the role of IU in anxiety disorders.

Similarly, fear of negative evaluation (FNE) has been considered a core characteristic of SP (Collins et al., 2005; Weeks et al., 2005; Moscovitch, 2009). Again, findings testing this assumption have been inconsistent. Collins et al. (2005) found that individuals with DSM-IV principal diagnoses of SP reported significantly greater FNE than individuals with principal diagnoses of PD. In contrast, findings of Oei and colleagues (1991) indicated that there were no significant differences in reported FNE across individuals with DSM-III diagnoses of SP, PD, and GAD alone. In each of these studies, however, individuals with additional, non-principal diagnoses were excluded from analyses, possibly obscuring the findings.

Finally, several studies have also compared levels of self-reported Anxiety Sensitivity (AS) across groups defined by principal anxiety disorder diagnoses. For instance, Taylor, Koch, and Crickett (1991) and Taylor, Koch, and McNally (1992) found that AS levels were higher in individuals with DSM-III principal diagnoses of PD compared to those with diagnoses of PTSD, GAD, OCD, SP, or specific phobias. Taylor et al. (1991) specifically compared individuals with PD alone to individuals with other principal anxiety diagnoses,

while Taylor et al. (1992) used a sample with very low rates of comorbidity [“10% of our panic disordered patients had an additional comorbid anxiety disorder...” p. 256]. Deacon and Abramowitz (2006) partially replicated these results in a clinical sample with moderate rates of comorbidity (34.1%), and comorbid diagnoses were ignored in the primary analyses. They reported that patients principally diagnosed with PD showed significantly elevated AS compared to patients principally diagnosed with either GAD or specific phobias, while patients with principal diagnoses of OCD or SP did not differ significantly from other groups, including PD. Given that comorbid presentations of the diagnoses of interest were excluded/ignored in all of these studies, caution should be taken before drawing conclusions. A meta-analysis by Naragon-Gainey et al. (2010) also compared AS across diagnostic groups of anxiety and mood disorders and also formulated diagnostic groups based on principal diagnoses, although analyses used path analysis to account for symptom-level overlap among diagnostic constructs. In contrast to Deacon and Abramowitz (2006), they found that AS was most strongly associated with PD, GAD, and PTSD.

Similar issues come to light in treatment outcome studies, particularly in transdiagnostic treatment trials comparing treatment efficacy across individuals with different diagnoses. Norton (2008), for example, compared treatment outcomes following a 12-week transdiagnostic group CBT program across treatment completers (55.8% rate of comorbidity) with DSM-IV principal diagnoses of PD, SP, and GAD, finding no evidence of differential improvement. Similarly, Schmidt et al. (2012) compared treatment outcomes following a 10-week transdiagnostic group CBT program across groups defined by DSM-IV principal anxiety disorder diagnoses despite reporting high rates of comorbid anxiety diagnoses. As with the Norton (2008) study, no evidence of differential outcomes was observed (Schmidt et al.).

The findings of some of these studies suggest no differences between those with differing principal anxiety disorders while others reported statistically significant differences. Interestingly, all of these studies reporting no significant differences included samples with comorbidity but ignored non-principal diagnoses and compared groups by principal diagnosis only. In contrast, the studies using “pure” samples with no or minimal rates of non-principal diagnoses reported differences across diagnoses. Therefore, the extent to which the nonsignificant results reflect actual non-differences versus differences masked by the presence of comorbid anxiety diagnoses is unclear. That is, are the lack of differences between principal diagnoses of A and B due, in part, to the possible presence of additional comorbid diagnoses of B and A, respectively? One inherent limitation of comparisons by principal diagnosis is that such analyses make the implicit assumption that, for example, an individual with a principal diagnosis of PD and a comorbid diagnosis of SP is categorically distinct from an individual with a principal diagnosis of SP and a comorbid diagnosis of PD [i.e., (PD+SP) ≠ (SP+PD)]. For the purposes of the current study, the term *hierarchically opposing diagnostic pairs* is used to refer to such clients who share the same diagnoses, but differ in terms of which diagnosis is considered “principal” versus “additional/comorbid.” The term “*opposing*” is used to denote the opposite hierarchical ordering of the diagnoses, and does not imply any contradiction or conflict between the diagnostic pairs.

Several attempts to compensate for additional, non-principal diagnoses in cross-diagnostic comparisons have been made, although each approach has significant limitations. Some studies (e.g., Collins et al., 2005; Oei et al., 1991; Taylor et al., 1991, 1992) have utilized samples with no or limited comorbid diagnoses to provide “pure” comparisons of each diagnostic group. While appealing on a face valid level, the fact that a majority of individuals with an anxiety disorder diagnosis will present with at least one additional anxiety disorder diagnosis (Brown and Barlow, 1992; Kroenke et al., 2007) calls into question the generalizability of results based on “pure” samples. Second, several studies (e.g., Barrera and Norton, 2009; Deacon and Abramowitz, 2006) have conducted secondary analyses to examine whether their primary results differed across those with or without any comorbid diagnoses. This approach is also limited as it fails to differentiate among the different specific comorbid diagnoses (e.g., PD+SP vs. SP+PD could be expected to be more overlapping than PD+GAD vs. SP+OCD). Some (e.g., Norton, 2008) have attempted to use factorial methods by coding participants as Yes/No for each diagnosis, although this method can yield small or empty cell sizes with smaller samples or a large number of diagnoses, thus potentially violating key assumptions of the statistical tests. Finally, some (e.g., Krueger & Markon, 2006) have suggested multivariate structural modeling approaches to disentangle shared versus unique sources of variable among comorbid diagnoses, although the utility of this approach in studies with smaller samples is questionable.

To our knowledge, only one study has included at least one pair of comorbid anxiety diagnoses when comparing anxiety-related phenomena. In a comparison of DSM-III diagnoses of SP alone, PD alone, and comorbid SP and PD, Ball and colleagues (1995) reported that patients with SP alone had significantly greater FNE than patients with PD alone and patients with comorbid SP and PD, although the hierarchical relationship of the SP and PD (principal or comorbid) was not specified. Furthermore, findings indicated a substantial degree of overlap in AS and catastrophic beliefs about panic attacks across those with SP alone, PD alone, and comorbid SP and PD.

Even in studies examining phenomena within a single anxiety disorder diagnosis, it appears to be common to define membership in the diagnostic group of interest without regard for comorbid diagnoses. Indeed, an informal review¹ of the past 16 issues published in the last year of the current journal suggested that roughly 7 studies (or approximately 0.44 per issue, on average) disregarded comorbid diagnoses and defined groups by primary diagnosis only, and only a total of 2 studies explicitly reported that they defined groups based on any presence of the diagnosis of interest (primary or comorbid). However, 12 studies did not report how diagnostic groups were defined. While the impact of such methodological decisions on study results is unclear, it is possible that the presence of additional anxiety diagnoses could attenuate or influence the resulting conclusions about the diagnosis of interest in these studies.

The purpose of the current study was, therefore, to examine the impact of multiple anxiety disorder comorbidity in comparison to individuals meeting criteria for only one anxiety

¹This review only included studies examining specific anxiety disorders and excluded meta-analyses, literature reviews, and studies that did not use standard diagnostic clinical interviews or clinical samples.

diagnosis. Specifically, we sought to investigate the extent to which hierarchically opposing diagnostic pairs showed similarities and differences from their non-comorbid counterparts, in an effort to better define the extent to which comparison by principal diagnoses are valid. It was hypothesized that non-comorbid and comorbid groups sharing the same diagnosis (A, A+B, and B+A) would score similarly and significantly higher on measures of that diagnosis than would the non-comorbid group not sharing the diagnosis (B) [e.g., $(A = (A+B) = (B + A)) > B$ on a measure of A]. Specifically, participants with principal or comorbid diagnoses of PD were expected to demonstrate higher scores on a measure of PD severity and a vulnerability factor variable associated with PD (AS), participants with principal or comorbid diagnoses of SP were expected to demonstrate higher scores on a measure of SP severity and a vulnerability factor variable associated with SP (FNE), and participants with principal or comorbid diagnoses of GAD were expected to demonstrate higher scores on a measure of GAS severity and a vulnerability factor variable associated with GAD (IU).

2. Methods

2.1 Participants

Client data were obtained from 459 community individuals presenting for treatment services at the University of Houston (UH) Anxiety Disorder Clinic. Participants were recruited for participation via advertisements and articles in local and neighborhood newspapers, referrals from health and mental health professions, and public service media announcements. The following criteria were established for inclusion in the study: (a) age 18 or older, (b) principal DSM-IV diagnosis of any anxiety disorder, (c) adequate proficiency in English, (d) no evidence of dementia or other neurocognitive conditions that would impair ability to provide informed consent or participate in treatment, and (e) absence of suicidality, serious substance abuse, or another condition requiring immediate intervention. Although some participants may have been current students at the university, the majority came from the broader Houston community.

Of the initial sample of 459, 51 met criteria for PD only (i.e., did not meet criteria for additional diagnoses of SP or GAD), 23 PD+SP, and 45 PD+GAD; 89 SP only (i.e., did not meet criteria for additional diagnoses of PD or GAD), 11 SP+PD, and 55 SP+GAD; and 19 GAD only (i.e., did not meet criteria for additional diagnoses of PD or SP), 22 GAD+PD, and 38 GAD+SP. Only the 353 participants in these categories were subsequently analyzed. Other comorbid diagnoses in the sample included depressive disorders (20%), specific phobia (4.9%) and OCD (3%), and substance use disorders (2.1%), with no other comorbid diagnoses occurring in greater than 2% of the current sample. The sample showed relatively even sex distribution (46.8% men, 53.2% women), and was somewhat racially diverse (54.7% Caucasian, 20.1% Hispanic/Latino, 10.3% African American, 7.3% Asian American, 4.3% other or mixed racial background, 0.3% Native American, 3.0% unreported). The sample ranged in age from 18 to 71 years old, with a mean of 32.82 ($SD = 10.47$). Most were single (53.2%) or married (31.9%), and were fairly well educated (33.7% some undergraduate, 28.9% Bachelor's degree or equivalent, 10.3% some professional/graduate school, 14.9% graduate/professional degree).

For analyses, multi-category demographic variables (i.e., race/ethnicity, marital status, occupational status) were dummy coded into dichotomous variables for inclusion as dependent variables in a multivariate analysis of variance (MANOVA) such that race/ethnicity was coded as 0 = White/European descent, non-Hispanic, 1 = non-White/European descent or Hispanic ethnicity; marital status was coded as 0 = married/cohabitating with partner, 1 = single, separated, or divorced; and occupational status was coded as 0 = full time employed, fulltime student, or fulltime homemaker, 1 = part time status or unemployed.²

2.2 Measures

All participants received a structured diagnostic assessment at intake, the Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV; Brown et al., 1994), including Axis I diagnoses (Axis II diagnoses were not assessed) and an Axis V Global Assessment of Functioning (GAF), and completed a battery of self-report measures assessing anxiety disorder severity and anxiety-related vulnerability factors.

2.2.1 Clinician-rated measures

2.2.1.1 Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV): The ADIS-IV (Brown et al., 1994) is a semi-structured diagnostic interview designed to assess the presence, nature, and severity of DSM-IV anxiety, mood, and somatoform disorders, as well as previous mental health history. The interview also contains a brief screen for psychotic symptoms, and alcohol or substance abuse. All ADIS-IV interviewers, advanced doctoral students, were trained to reliability standards by observing an interview conducted by an experienced interviewer then conducting at least three interviews under observation. Data obtained from the ADIS-IV for this study included Axis I principal and comorbid diagnoses, as well as Axis V GAF (Endicott et al., 1976) scores. A large scale analysis of the ADIS-IV offers strong support for the reliability of diagnoses using the ADIS-IV (Brown et al., 2001), and the current data showed a high degree of diagnostic agreement across primary (86% agreement; $\kappa = 0.77$) and comorbid diagnoses (75% agreement; $\kappa = 0.71$) using blind reliability raters (see Norton 2012; Norton and Barrera, 2012). Principal diagnoses were defined by the interviewer as the most severe and disabling diagnosis, while comorbid diagnoses were assigned if the client met criteria for an additional diagnosis of lesser but clinically significant severity.

2.2.2 Self-report diagnostic measures of anxiety severity

2.2.2.1 Panic Disorder Severity Scale (PDSS): The PDSS (Houck et al., 2002) is a 7-item self-report measure of PD severity. Each item is on a 5-point Likert scale, ranging from 0 to 4, with higher ratings indicating higher severity for each item. The PDSS has demonstrated good reliability and validity in panic disordered and psychiatric outpatients (Shear et al., 1997; Shear et al., 2001; Houck et al., 2002) and excellent internal consistency in the current sample ($\alpha = 0.954$).

²Univariate analyses using the dichotomized/dummy-coded vs. multi-category variables showed no differences in association with the diagnostic group variables; however limited cell counts and *df* considerations suggested the use of the dummy-coded variables.

2.2.2.2 Social Phobia Diagnostic Questionnaire (SPDQ): The SPDQ (Newman et al., 2003) is a 25-item self-report measure of the symptomology and severity of SP. Eighteen items are on a 5-point Likert scale, ranging from 0 (*No fear or Never avoid*) to 4 (*Very severe or Always avoid*), and 7 items are dichotomous (i.e., Yes/No) questions (e.g., *Do you try to avoid social situations?*). The SPDQ has shown excellent psychometric properties (Newman et al., 2003) and strong internal consistency in the current sample ($\alpha = 0.868$).

2.2.2.3 Generalized Anxiety Disorder Questionnaire- IV (GADQ-IV): The GADQ-IV (Newman et al., 2002) is a 9-item self-report diagnostic measure of GAD based on the DSM-IV. Item structures range from dichotomous questions (e.g., *Do you experience excessive worry?*) to free response questions (e.g., *Please list the most frequent topics about which you worry excessively or uncontrollably*) to 9-point Likert type scales, ranging from 0 (*None*) to 8 (*Very Severe*). The GADQ-IV has demonstrated good psychometric properties among samples with GAD, other anxiety disorders, and non-anxious controls (Newman et al., 2002) and strong internal consistency in the current sample ($\alpha = 0.805$).

2.2.3 Measures of anxiety-related underlying vulnerability factors

2.2.3.1 Anxiety Sensitivity Index (ASI): The ASI (Reiss et al., 1986) is a 16-item self-report measure of AS, or the extent to which individuals fear anxiety-related symptoms and their consequences. Each item is rated on a 5-point Likert scale, ranging from 1 (*very little*) to 5 (*very much*), with higher scores indicating greater AS. The ASI has demonstrated adequate psychometric properties (Reiss et al., 1986) and strong internal consistency in the current sample ($\alpha = 0.795$).

2.2.3.2 Intolerance of Uncertainty Scale (IUS): The IUS (Sexton and Dugas, 2009) is a 27-item self-report measure of the degree to which respondents view uncertainty as intolerable. All items are rated on a 5-point Likert scale, ranging from 1 (*not at all characteristic of me*) to 5 (*entirely characteristic of me*). The total score is calculated by summing all items. Higher scores indicated greater IU. Studies have indicated that the IUS has sound psychometric properties (Khawaja and Yu, 2010; Sexton and Dugas, 2009) and the current sample showed strong internal consistency ($\alpha = 0.897$).

2.2.3.3 Brief Fear of Negative Evaluation Scale (BFNE): The BFNE (Leary, 1983) is a 12-item self-report measure of the extent to which respondents fear negative evaluation from others. Each item is rated on a 5-point Likert scale, ranging from 1 (*not at all characteristic of me*) to 5 (*extremely characteristic of me*). The BFNE has demonstrated optimal psychometric properties (Collins et al., 2005; Leary, 1983) and strong internal consistency in the current sample ($\alpha = 0.866$).

2.3 Procedure

All assessments were conducted at the UH Anxiety Disorder Clinic. All methods and procedures were reviewed by the UH Institutional Review Board. All potential participants underwent a brief telephone screen to provide initial evidence of suitability for a larger treatment study. Potential participants who appeared to be eligible for participation were

scheduled for the structured diagnostic evaluation. Informed consent was obtained from all participants. Treatment services were self-pay at a reduced rate.

2.4 Analytic Strategy

To test for differences among the principal-only and comorbid groups, for each set of outcomes a series of MANOVAs were constructed to compare participants across the four combinations of each of the following principal or comorbid diagnoses: (1) PD and SP (e.g., PD-only, PD+SP, SP+PD, SP-only), (2) PD and GAD, and (3) SP and GAD. Where omnibus effects were observed, *post-hoc* Bonferroni-corrected tests were conducted to explore whether the hypothesized pattern of results was obtained versus an unexpected pattern of differences.

3. Results

3.1 Associations among Demographic Characteristics

The first set of MANOVAs compared groups across demographic variables of age, sex, race, marital status, and occupational status. As hypothesized, no significant multivariate demographic relationships emerged differentiating participants diagnosed as PD, PD+SP, SP+PD, or SP, $F(15,483) = 0.93, p = 0.53$, Pillai = 0.085, partial $\eta^2 = 0.027$; PD, PD+GAD, GAD+PD, or GAD, $F(15,378) = 0.97, p = 0.49$, Pillai = 0.111, partial $\eta^2 = 0.030$; or SP, SP+GAD, GAD+SP, or GAD, $F(15,573) = 1.19, p = 0.27$, Pillai = 0.091, partial $\eta^2 = 0.037$. Therefore, no demographic variables were entered as covariates in any of the subsequent analyses.

3.2 Associations among Clinician-Rated Psychosocial Functioning

The second set of MANOVAs compared groups on clinician-rated Axis V Global Assessment of Functioning scores. As hypothesized, significant differences in GAF scores emerged between participants diagnosed with PD, PD+SP, SP+PD, or SP; participants diagnosed as PD, PD+GAD, GAD+PD, or GAD; or participants diagnosed as SP, SP+GAD, GAD+SP, or GAD. In each analysis, Bonferroni-corrected post-hoc tests indicated that comorbid participant groups did not differ significantly from each other but scored significantly lower (more impaired) than the non-comorbid groups, who did not differ (Table 1).

3.3 Associations among Client Reported Anxiety Symptoms

The third set of MANOVAs compared groups on self-reported anxiety disorder symptoms on the PDSS, SPDQ, and GADQ-IV. In comparing participants diagnosed as principal or additional PD or SP, a significant multivariate effect was observed. Bonferroni-corrected post-hoc examination of the univariate effects suggested that, as hypothesized, this difference was driven by significant differences on the PDSS, $F(3,112) = 10.39, p < 0.001$, partial $\eta^2 = 0.222$, SPDQ, $F(3,112) = 49.58, p < 0.001$, partial $\eta^2 = 0.577$, and GADQ-IV, $F(3,112) = 9.03, p < 0.001$, partial $\eta^2 = 0.199$. On the PDSS, consistent with the hypothesis, participants with any principal or additional PD diagnosis did not differ from each other but scored significantly higher than those diagnosed as SP only. Similarly, on the SPDQ the results were consistent with the hypothesis that participants diagnosed with any principal or

additional SP did not differ from each other but scored significantly higher than did those diagnosed as PD only. Finally, GADQ-IV results suggested that both comorbid groups (PD +SP and SP+PD) did not differ from each other but scored significantly higher than did PD or SP, who did not differ from each other (Table 2).

Comparisons of principal or additional PD or GAD yielded a significant multivariate effect. Bonferonni-corrected post-hoc tests examination of the univariate effects suggested that, as hypothesized, this difference was driven by significant differences on the PDSS, $F(3,89) = 10.43, p < 0.001$, partial $\eta^2 = 0.260$, SPDQ, $F(3,89) = 6.91, p < 0.001$, partial $\eta^2 = 0.189$, and GADQ-IV, $F(3,89) = 12.24, p < 0.001$, partial $\eta^2 = 0.292$. On the PDSS, consistent with the hypothesis, participants with any principal or additional PD diagnosis did not differ from each other but scored significantly higher than those diagnosed as GAD only. Similarly, on the GADQ-IV the results were consistent with the hypothesis that participants diagnosed with any principal or additional GAD did not differ from each other but scored significantly higher than did those diagnosed as PD only. SPDQ results suggested that both comorbid groups (PD+GAD and GAD+PD) did not differ from each other but scored significantly higher than did the PD only group. Only the PD+GAD group scored significantly higher than the GAD group, with the difference between the GAD+PD and GAD groups not being statistically significant ($p = 0.078$). The PD and GAD groups did not differ from each other (Table 2).

Finally, the comparison of principal or additional SP or GAD also revealed a significant multivariate effect. Bonferonni-corrected post-hoc examination of the univariate effects suggested that, as hypothesized, this difference was driven by significant differences on the SPDQ, $F(3,142) = 31.06, p < 0.001$, partial $\eta^2 = 0.396$, and GADQ-IV, $F(3,142) = 31.78, p < 0.001$, partial $\eta^2 = 0.402$, but not the PDSS $F(3,142) = 1.80, p = 0.15$, partial $\eta^2 = 0.037$. On the SPDQ, consistent with the hypothesis, participants with any SP diagnosis did not differ from each other but scored significantly higher than those diagnosed as GAD only. Similarly, on the GADQ-IV the results were consistent with the hypothesis that participants diagnosed with any principal or additional GAD did not differ from each other but scored significantly higher than did those diagnosed as SP only (Table 2).

3.4 Associations among Self-Reported Underlying Vulnerability Factors

The final set of MANOVAs examined potential differences in self-reported vulnerability factor variables associated using the ASI, IUS and BFNE. In the first MANOVA comparing participants diagnosed as principal or additional PD or SP, a significant multivariate effect was observed. Bonferonni-corrected post-hoc examination of the univariate effects suggested that, as hypothesized, this difference was driven by significant differences on the ASI, $F(3,114) = 3.42, p = 0.02$, partial $\eta^2 = 0.082$, IUS, $F(3, 114) = 14.86, p < 0.001$, partial $\eta^2 = 0.281$, and BFNE, $F(3, 114) = 24.06, p < 0.001$, partial $\eta^2 = 0.388$. On the ASI, generally consistent with the hypothesis, participants with any principal or additional PD diagnosis did not differ from each other but scored significantly higher than those diagnosed as SP only, with the exception that the difference between SP and PD+SP did not reach significance, $p = 0.059$. Similarly, on the BFNE the results were consistent with the hypothesis that participants diagnosed with any principal or additional SP did not differ from

each other but scored significantly higher than did those diagnosed as PD only. Finally, IUS results suggested that both comorbid groups (PD+SP and SP+PD) did not differ from each other but scored significantly higher than did SP, who in turn scored significantly higher than those diagnosed as PD (Table 3).

In the second MANOVA comparing participants diagnosed as principal or additional PD or GAD, a significant multivariate effect was observed. Bonferonni-corrected post-hoc examination of the univariate effects suggested that, as hypothesized, this difference was driven by significant differences on the ASI, $F(3,96) = 5.40, p = 0.002$, partial $\eta^2 = 0.144$, IUS, $F(3, 96) = 19.94, p < 0.001$, partial $\eta^2 = 0.384$, and BFNE, $F(3, 96) = 7.31, p < 0.001$, partial $\eta^2 = 0.186$. On the ASI, generally consistent with the hypothesis, participants with any PD diagnosis did not differ from each other but scored significantly higher than those diagnosed as GAD only, with the exception that the difference between GAD and PD did not reach significance, $p = 0.077$. On the IUS, the results were somewhat consistent with the hypothesis. Participants diagnosed with any principal or additional GAD scored significantly higher than did those diagnosed as PD only, although the two comorbid groups (PD+GAD and GAD+PD) scored significant higher than did the GAD group. Finally, BFNE results suggested that only the PD+GAD group scored significantly higher than did those diagnosed as PD (Table 3).

In the final MANOVA comparing participants diagnosed as principal or additional SP or GAD, a significant multivariate effect was observed. Bonferonni-corrected post-hoc examination of the univariate effects suggested that, as hypothesized, this difference was driven by significant differences on the IUS, $F(3,143) = 15.23, p < 0.001$, partial $\eta^2 = 0.242$, and BFNE, $F(3,143) = 4.61, p = 0.004$, partial $\eta^2 = 0.088$, but not the ASI, $F(3,143) = 2.72, p = 0.05$, partial $\eta^2 = 0.054$. On the IUS, contrary to the hypothesis, comorbid participants (SP+GAD and GAD+SP) did not differ from each other but scored significantly higher than those diagnosed as either GAD or SP. On the BFNE, the results were consistent with the hypothesis that participants diagnosed with any principal or additional SP did not differ from each other but scored significantly higher than did those diagnosed as GAD (Table 3).

4. Discussion

The current study aimed to examine the extent to which hierarchically opposing diagnostic pairs showed similarities and differences from their non-comorbid counterparts on clinician-rated functioning, specific diagnostic features of the respective principal diagnoses, underlying vulnerability factors (e.g., IU, AS, FNE), and demographic characteristics. Overall, two generally consistent themes emerged from the results. First, groups with comorbid anxiety diagnoses typically showed greater impairment over “pure” anxiety disordered individuals as assessed by clinician GAF scores and measures of unrelated diagnostic features. The finding of greater functional impairment is consistent with some research (for a review see Mathew et al., 2013; but cf. Olatunji et al., 2010).

However, the elevations among the comorbid groups on unrelated measures were unexpected. That is, it is unclear why the PD+GAD and GAD+PD groups scored higher than the PD or GAD groups on a measure of SP, or why the SP+PD and PD+SP groups

would score higher than the PD or SP groups on a measure of GAD, for example. It is possible that the diagnosticians in the current study felt that additional features were sufficiently subsumed under the principal and comorbid diagnosis that an additional diagnosis was not warranted. However, it may also be that individuals with anxiety comorbidity are stronger representations of the inherent limitations of a categorical diagnostic system and are likely to show elevations across a range of anxiety indices than are individuals who do fit more neatly into the nosological structure. Indeed, it may also be that those with more than one disorder tend to have higher levels of neuroticism, as neuroticism is strongly linked to sources of comorbidity (Khan, Jacobson, Gardner, Prescott, & Kendler, 2005) and, possibly, symptoms and features of multiple diagnoses. Keeley and Blashfield (2010) also suggested that comorbid combinations of pathology may produce characteristics/symptoms that extend beyond the expected areas of each specific condition. In using the example above, an individual with PD+GAD may exhibit panic symptoms (from PD), worry (from GAD), and FNE (similar to SP). While it is possible that this phenomenon may explain the current study's finding, research should further explore the validity of this process.

Second, consistent with our hypotheses and in accordance with an additive model of diagnostic comorbidity (Keeley et al., 2013), the presence of an anxiety disorder diagnosis (principal or comorbid) was associated with greater elevations on measures of that diagnostic construct than was seen among those without that diagnosis. Symbolically, this would be represented as $[A = (A+B) = (B+A)] > B$ on a measure of A, but $A < [(A+B) = (B+A) = B]$ on a measure of B. This finding has significant implications for cross-diagnostic comparison studies, as the relatively common practice of ignoring non-principal diagnoses and comparing across principal diagnoses appears unjustifiable given the current data. Indeed, the influence of comorbid diagnoses may attenuate, or even negate, actual differences across diagnoses, as many of the previously reviewed studies reporting differences by principal diagnosis used non-comorbid samples while those reporting no significant differences typically utilized samples where comorbid diagnoses were present but ignored in the primary analyses. Thus, future research making cross-diagnostic comparisons should make efforts to include comorbid presentations of the diagnoses of interest and report comorbid presentations in greater detail, rather than selecting groups based on principal diagnoses. Unfortunately, several potential solutions for statistically accounting for comorbidity each have limitations. One approach that may be promising given the current data is to employ a factorial approach [diagnosis A (yes/no), diagnosis B (yes/no)], although caution must be taken to avoid small or empty cell sizes that may violate the assumptions of the statistical tests. More research into statistical methods that account for the potential (but not necessary) presence of overlapping and distinct comorbid diagnoses is clearly warranted.

Findings of the current study may also raise questions regarding the continued use of the hierarchical additive model of DSM diagnoses, at least in regard to the anxiety disorders. While the results of the present study do not directly contest the use of hierarchical diagnoses by DSM in research and clinical practice, they do raise consideration of the limits of selecting or assigning groups based primarily on principal diagnoses when comorbidity is present, as the findings discredit the assumption that disorder A+B is different than disorder

B+A (e.g., PD + GAD = GAD + PD). Therefore, disregarding the apparent overlap between hierarchically opposing diagnostic combinations of anxiety disorders may be misleading, suggesting that it would be prudent for anxiety researchers not to follow practices of selecting/assigning groups based on principal diagnoses or omitting data because the diagnoses of interest are comorbid instead of principal.

Additionally, the dimensional overlap between comorbid presentations in the current study may provide support for recently proposed hybrid models of classification, which combine the use of categorical and dimensional approaches to classifying disorders (Brown and Barlow, 2009; Gros et al., 2013). Such approaches may help account for the wide spread comorbidity and dimensional overlap between the anxiety disorders, as well as between anxiety and depressive disorders (Brown and Barlow; Gros et al.). Furthermore, such approaches may attenuate problems caused by using a hierarchical model of comorbidity by placing greater acknowledgment on comorbid features outside of the principal diagnosis.

Of note, the present study did have certain limitations. For instance, we were unable to include every anxiety-related vulnerability factor shown to be implicated in anxiety disorders (e.g., worry, thought-action fusion) in the analyses, but we selected factors that appeared to be empirically supported and related to the anxiety disorders of interest in the study. Concerns exist regarding the psychometric properties of the GAF (e.g., Aas, 2011), and no inter-rater reliability data were collected in the current study on that measure, so caution should be taken in interpreting those results. Similarly, we did not include anxiety related diagnoses other than PD, SP, and GAD due to limitations of data availability. Therefore, it is unclear whether the results of the current study may generalize to other anxiety and related disorders (e.g., OCD, PTSD). Similarly, as only anxiety diagnoses were included, the current findings should not be automatically extended to comorbidity across or within other broad diagnostic classifications (e.g., Mood Disorders, Eating Disorders). Finally, some of the comorbid groups (e.g., SP+PD) were relatively under-represented in the current sample; future research should endeavor to recruit more robust samples representing each comorbid and non-comorbid group.

Limitations aside, in answering the question posed in the title, *Is a Gin and Tonic More Like Gin or Tonic?*, the findings of the current study appear to indicate that while the metaphorical gin and metaphorical tonic may be different from each other independently, a gin and tonic is as “gin-y” as gin and as “tonic-y” as tonic, and possibly more intense than either alone in some ways. This may pose a dilemma, as research and the DSM has traditionally considered hierarchically opposing anxiety disorder diagnostic pairs as distinct and separate entities based on their principal diagnoses. As discussed previously, many research studies comparing phenomena across anxiety disorders tends to either ignore or specifically exclude non-principal, comorbid diagnoses, drawing conclusions based on comparisons of principal diagnoses only. However, findings of the current study suggest that analyzing comparisons based on principal diagnoses may not be a valid procedure and may obscure research findings and interpretations.

Acknowledgments

The data reported in the current study was collected while supported (PJN) by an NIMH Mentored Research Scientist Development Award (MH073920) and University of Houston Grant to Enhance and Advance Research award.

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- We investigated the degree to which pairs of clients who share the same set of diagnoses, but differ in terms of principal diagnosis (i.e., hierarchically opposing diagnostic pairs) showed similarities and differences from their non-comorbid, or “pure,” counterparts.
- 353 participants with diagnoses of either Panic Disorder only, Social Phobia only, Generalized Anxiety Disorder only, or some comorbid pair of the three were examined.
- Findings indicated that hierarchically opposing diagnostic pairs showed more overlap than differentiation with each other and with non-comorbid counterparts.
- Thus, defining group comparisons by principal diagnoses may be invalid and misleading.

Table 1
Comparisons of Comorbid and Non-Comorbid Pairs by Clinician-Assessed Global Functioning

	Diagnostic Group			Omnibus Test Statistic
	PD (<i>n</i> = 51)	PD+SP (<i>n</i> = 23)	SP+PD (<i>n</i> = 11)	SP (<i>n</i> = 89)
GAF	63.24 (7.91) ^a	57.70 (11.43) ^b	57.45 (11.62) ^b	64.36 (8.32) ^a
				$F_{(3,170)} = 4.80$ $p = 0.003$ partial $\eta^2 = 0.078$
	PD (<i>n</i> = 51)	PD+GAD (<i>n</i> = 45)	GAD+PD (<i>n</i> = 22)	GAD (<i>n</i> = 19)
GAF	63.24 (7.91) ^a	56.60 (9.15) ^b	56.45 (7.68) ^b	66.21 (5.53) ^a
				$F_{(3,133)} = 10.54$ $p < 0.001$ partial $\eta^2 = 0.192$
	SP (<i>n</i> = 89)	SP+GAD (<i>n</i> = 55)	GAD+SP (<i>n</i> = 38)	GAD (<i>n</i> = 19)
GAF	64.36 (8.32) ^a	59.45 (9.41) ^b	60.68 (8.30) ^b	66.21 (5.53) ^a
				$F_{(3,197)} = 5.67$ $p = 0.001$ partial $\eta^2 = 0.079$

Note. PD = Panic Disorder; SP = Social Phobia; GAD = Generalized Anxiety Disorder; GAF = Global Assessment of Functioning.

^{a,b,c} Means not sharing the same superscript differ significantly at $p < 0.05$ or lower.

Table 2
 Comparisons of Comorbid and Non-Comorbid Pairs by Self-Reported Symptoms Severity

	Diagnostic Group			Omnibus Test	
	PD	PD+SP	SP+PD	SP	Statistic
PDSS	14.79 (4.42) ^a	14.38 (6.02) ^a	16.33 (5.87) ^a	8.81 (6.61) ^b	$F_{(9,327)} = 15.60$ $p < 0.001$
SPDQ	6.21 (5.74) ^a	17.31 (5.53) ^b	22.03 (2.98) ^b	18.15 (4.61) ^b	
GADQ-IV	17.85 (8.62) ^a	26.00 (5.97) ^b	23.22 (7.53) ^b	14.02 (8.88) ^a	partial $\eta^2 = 0.300$
	PD	PD+GAD	GAD+PD	GAD	
PDSS	14.79 (4.41) ^a	17.29 (5.60) ^a	13.73 (6.66) ^a	8.06 (5.18) ^b	$F_{(9,367)} = 8.03$ $p < 0.001$
SPDQ	6.21 (5.74) ^a	13.14 (7.52) ^b	12.38 (7.41) ^{bc}	8.19 (5.42) ^{ac}	
GADQ-IV	17.85 (8.62) ^a	27.64 (5.43) ^b	25.67 (5.69) ^b	23.69 (3.84) ^b	partial $\eta^2 = 0.213$
	SP	SP+GAD	GAD+SP	GAD	
PDSS	8.81 (6.61) ^a	11.41 (6.46) ^a	10.13 (6.53) ^a	8.06 (5.18) ^a	$F_{(9,426)} = 17.80$ $p < 0.001$
SPDQ	18.15 (4.61) ^a	20.77 (4.02) ^a	17.08 (4.43) ^a	8.19 (5.42) ^b	
GADQ-IV	14.02 (8.88) ^a	25.11 (5.92) ^b	26.00 (3.54) ^b	23.69 (3.84) ^b	partial $\eta^2 = 0.273$

Note. PD = Panic Disorder; SP = Social Phobia; GAD = Generalized Anxiety Disorder; PDSS = Panic Disorder Severity Scale; SPDQ = Social Phobia Diagnostic Questionnaire; GADQ-IV = Generalized Anxiety Disorder Questionnaire-IV.

^{a,b,c} Means not sharing the same superscript differ significantly at $p < 0.05$ or lower.

Table 3
Comparisons of Comorbid and Non-Comorbid Pairs by Self-Reported Underlying Vulnerability Factors

	Diagnostic Group				Omnibus Test	
	PD	PD+SP	SP+PD	SP	Statistic	
ASI	32.86 (10.34) ^a	33.79 (12.19) ^a	37.11 (11.20) ^a	27.02 (12.84) ^b	$F_{(9,342)} = 10.81$	
IUS	56.24 (18.06) ^a	96.36 (25.06) ^b	93.11 (27.80) ^b	69.03 (20.41) ^c	$p < 0.001$	
BFNE	34.78 (9.89) ^a	49.29 (12.39) ^b	53.33 (9.39) ^b	50.52 (8.35) ^b	partial $\eta^2 = 0.221$	
	PD	PD+GAD	GAD+PD	GAD		
ASI	32.86 (10.34) ^{ab}	39.55 (10.61) ^a	37.27 (10.59) ^a	27.18 (12.59) ^b	$F_{(9,288)} = 6.69$	
IUS	56.24 (18.06) ^a	92.45 (24.43) ^b	91.67 (24.47) ^b	71.41 (17.72) ^c	$p < 0.001$	
BFNE	34.78 (9.89) ^a	47.03 (9.88) ^b	41.83 (12.47) ^{ab}	42.47 (13.18) ^{ab}	partial $\eta^2 = 0.173$	
	SP	SP+GAD	GAD+SP	GAD		
ASI	27.02 (12.84) ^a	33.62 (11.73) ^a	30.26 (11.63) ^a	27.18 (12.59) ^a	$F_{(9,429)} = 5.71$	
IUS	69.03 (20.41) ^a	95.27 (26.49) ^b	94.48 (23.86) ^b	71.41 (17.72) ^a	$p < 0.001$	
BFNE	50.52 (8.35) ^a	52.17 (7.88) ^a	52.26 (12.37) ^a	42.47 (13.18) ^b	partial $\eta^2 = 0.107$	

Note. PD = Panic Disorder; SP = Social Phobia; GAD = Generalized Anxiety Disorder; ASI = Anxiety Sensitivity Index; IUS = Intolerance of Uncertainty Scale; BFNE = Brief Fear of Negative Evaluation Scale.

^{a,b,c} Means not sharing the same superscript differ significantly at $p < 0.05$ or lower.