Comorbidity of Personality Disorders in Anxiety Disorders: A Meta-Analysis of 30 Years of Research

Oddgeir Friborg [1, 2]

Monica Martinussen [3]

Sabine Kaiser [1]

Karl Tore Øvergård [1]

Jan H. Rosenvinge [1]

[1] Faculty of Health Sciences, Department of Psychology, University of Tromsø, Norway.

[2] Psychiatric Research Centre of Northern Norway, University Hospital of Northern Norway, Tromsø.

[3] Faculty of Health Sciences, Regional Centre for Child and Youth Mental Health and Child Welfare, University of Tromsø, Norway.

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Corresponding author

Oddgeir Friborg
University of Tromsø
Faculty of Health Sciences
Department of Psychology
N-9037 Tromsø, Norway.
Email: oddgeir.friborg@uit.no
Phone: +47 776 46 772
Fax: +47 776 45 291

Abstract

Background. A comprehensive meta-analysis to identify the proportions of comorbid personality disorders (PD) across the major subtypes of anxiety disorders (AD) has not previously been published.

Methods. A literature search identified 125 empirical papers from the period 1980-2010 on patients with panic disorders, social phobia, generalised anxiety, obsessive-compulsive (OCD) and post-traumatic stress disorder (PTSD). Several moderators were coded.

Results. The rate of any comorbid PD was high across all ADs, ranging from .35 for PTSD to .52 for OCD. Cluster C PDs occurred more than twice as often as cluster A or B PDs. Within cluster C the avoidant PD occurred most frequently, followed by the obsessive-compulsive and the dependent PD. PTSD showed the most heterogeneous clinical picture and social phobia was highly comorbid with avoidant PD. A range of moderators were examined, but most were non-significant or of small effects, except an early age of onset, which in social phobia increased the risk of an avoidant PD considerably. Gender or duration of an AD was not related to variation in PD comorbidity.

Limitations. Blind rating of diagnoses was recorded from the papers as an indication of diagnostic validity. However, as too few studies reported it the validity of the comorbid estimates of PD was less strong.

Conclusions. The findings provided support to several of the proposed changes in the forthcoming DSM-5. Further comorbidity studies are needed in view of the substantial changes in how PDs will be diagnosed in the DSM-5.

Words: 237

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Comorbidity of Personality Disorders in Anxiety Disorders: A Meta-Analysis of 30 Years of Research

Anxiety disorders (ADs) are one of the most common mental disorders with a 12-month prevalence of 18% and a lifetime prevalence of about 30% (Kessler et al., 2005a; Kessler et al., 2005b). Depending on the nature and severity of an AD, the concurrent debilitation of daily functioning and quality of life may become substantial (Ghaedi et al., 2010; Lochner et al., 2003). As avoidance of situations and/or other people are the cardinal behavioural symptoms of ADs, the immobilisation and isolation tend to increase over time. This eventually impedes the quality of social relationships and support (Hickey et al., 2005; Stein and Kean, 2000), which in combination with the primary AD symptoms contribute to the chronic course of the disorder (Beard et al., 2010; Perkonigg et al., 2005; Rubio and Lopez-Ibor, 2007; Wittchen, 2002), particularly if left untreated.

The comorbidity of other mental disorders appears to be the rule rather than an exception (Barlow et al., 1986), which partly derives from the secondary functional problems arising over time. In a study by Sanderson, DiNardo, Rapee and Barlow (1990), up to 70% of the patients had at least one additional axis I diagnosis. The high comorbidity is striking. However, such estimates may be inflated as the current diagnostic system (i.e., DSM-IV or ICD-10) largely neglects communality in symptom clusters across diagnostic groups. Nevertheless, mental disorder comorbidity is considered negative for the natural course of illness by implying additional kinds of dysfunction (Coryell et al., 1988) depending on whether it is a disorder of mood, substance abuse or personality (Ansell et al., 2011; Brown and Barlow, 1992). These three are the most common comorbid disorders.

Comorbid depression mainly involves anhedonia and reduced motivation. Such clinical features may strongly temper the effects of treatment (Spijker et al., 2001), and in

particular psychotherapy treatments requiring own efforts, such as behavioural homework tasks commonly used in for instance cognitive-behavioural therapy. A substance abuse disorder may represent a coping behaviour strategy and a negative reinforcement factor counteracting change in automated avoidance behaviour. This paper focuses however on the proportions of comorbidity of axis II personality disorders (PD). Such comorbidity may more profoundly affect the prognosis and outcome of an AD compared to any other axis I comorbid diagnoses (Reich, 2003; Telch et al., 2011).

One distinction between axis I and II comorbid disorders seems to be in terms of severity and complexity. First, the degree of fear and phobic avoidance (Dreessen et al., 1994; Kose et al., 2009) is usually more pronounced in patients with axis II compared with axis I comorbidity, as well as the level of general psychopathology (Dreessen et al., 1994; Ozkan and Altindag, 2005). This is also reflected in analyses of health care costs showing that axis II PD patients represent a markedly higher economic burden to the health care system than for example depression and anxiety patients (Soeteman et al., 2008). Moreover, having a PD represents a strong vulnerability factor for developing other axis I disorders (Stein et al., 1993). Second, treatment of comorbid PDs are normally more complex and less optimistic than treatment of axis I comorbidities due to less favourable outcomes (Reich, 2003; Slaap and den Boer, 2001; Telch et al., 2011), higher drop-out rates (Sanderson et al., 2002), less positive patient expectations (Martino et al., 2012) and more challenges with establishing a durable and flexible therapeutic alliance (Bienenfeld, 2007; Martino et al., 2012). Furthermore, the degree of comorbid psychosocial impairment depends on the type of PD. For example in a study of 668 PD patients, Skodol et al. (2002) reported a higher degree of impairment among schizotypal and borderline patients than among obsessive-compulsive or avoidant PD patients.

Several reviews of general associations between PDs and ADs have been published (Bienvenu and Stein, 2003a; Brandes and Bienvenu, 2009; Brooks et al., 1989; Stein et al., 1993; Van Velzen and Emmelkamp, 1999). The general conclusions from these reviews are that the comorbid frequency of PDs among patients with an AD diagnosis vary considerably, but that the proportions are highest in the avoidant, dependent and compulsive PDs (cluster C), and smaller in the schizoid, schizotypal and paranoid PDs (cluster A) and the dramatic, borderline and anti-social PDs (cluster B). Patients with cluster A or cluster B PDs also appear to have a poorer treatment response than cluster C PD patients (Hansen et al., 2007; Noyes et al., 1990).

Very few meta-analyses on the same comorbidity have been published. To the best of our knowledge there is only one previous meta-analysis by Ng and Borenstein (2005). They specifically examined the comorbidity of a dependent PD (mean r = .11). However, the ratio varied considerably between AD diagnostic groups, with panic disorder, obsessive-compulsive disorder (OCD), agora- and social phobia showing a higher prevalence of PD, while generalised anxiety disorder (GAD) and post-traumatic stress disorder (PTSD) showed no relationship with PD. The study was also criticised (Holmbeck and Durlak, 2005) for using a PD rather than an AD as the main inclusion criteria. The lack of previous meta-analyses using AD as the prime inclusion criteria, as well as studies that summarises the comorbidity of a PD across all AD diagnostic groups was therefore the main impetus for the present study. Additionally, we present data as proportions (equal to percentages), which represents a more user-friendly and intuitive effect size statistic.

Associated dysfunctions with PD and expected rates of comorbidity across the AD diagnoses

The patterns of dysfunction and severity of a comorbid PD depend of the type of PD (Ansell et al., 2011). Panic disorder patients with or without agoraphobia are usually strongly confined to their home due to rigid avoidance of public, enclosed or open spaces (Rodriguez et al., 2007), hence constricting mobility and social participation. As avoidance is one of the core symptoms of a panic disorder, the avoidant PD is also one of the most frequent comorbid PDs (Brooks et al., 1989). An avoidant personality preference easily intensifies the primary anxiety problems due to the loss of exposure to potentially corrective experiences. A dependent PD is less common, but if present, the patient may develop an undue reliance on another person, hence representing a safety behaviour strategy. The undue reliance also affects reciprocity in the relationships with other people, which over time constrict the social network. Patients with a borderline PD have more intense panic attacks, and they also attract a lot more attention and concern from other people. It is also regarded as the single PD with the poorest prognosis for a successful treatment of a panic attack disorder (Nurnberg et al., 1989).

Patients with social phobia are overly afraid of negative evaluations and social embarrassments. Hence, they avoid or at least endure with great pain any situations that involve visibility or responsibility. The protracted avoidance and social withdrawal is also presumed as the prime reason for the lower socioeconomic status often characterizing this group (Stein and Kean, 2000; Vorcaro et al., 2004). The avoidant PD is the most frequently occurring comorbid condition (Tillfors and Ekselius, 2009), which is expected considering the strong phenomenological overlap between these two diagnoses (Brooks et al., 1989; Reich, 2000; Rettew, 2000). However, in a review by Rettew (2000) the comorbidity estimates varied extremely, from 25% to nearly 100%. Clearly, this variation must be due to other factors than sampling error alone. Hence, we expected the avoidant PD to be most prevalent comorbid PD in social phobia. Moreover, this PD is particularly related to a poor treatment outcome (Turner, 1987).

Patients with GAD experience constant worry and tension as their prime symptoms. Procrastination, avoidance behaviour and frequent reassurance seeking from others are typical compensatory strategies (Clark and Beck, 2010). Patients with social phobia and GAD appears to have higher rates of comorbidity than patients with panic disorders (Blashfield et al., 1994; Jansen et al., 1994). Cluster C PDs appears to be the most prevalent in GAD, particularly the avoidant and the OCD PD subtypes (Garyfallos et al., 1999). We therefore expected these to have the highest comorbid estimates. Like for social phobia, the avoidant PD also appear to be the most relevant PD predicting a poorer treatment outcome (Massion et al., 2002).

PTSD-patients are particularly prone to lapse into unhealthy behaviours by overusing alcohol or drugs to alleviate traumatic memories (Hidalgo and Davidson, 2000; Leeies et al., 2010), which over time leads to a poorer physical health and an overuse of health care services (Greenberg et al., 1999). A connection between PTSD and the axis II disorders avoidant (Ansell et al., 2011), obsessive-compulsive (Pietrzak et al., 2011) and borderline PDs have been established (Bienvenu and Stein, 2003b; Pagura et al., 2010; Shea et al., 1999), but also with paranoid and schizotypal PDs (Crepulja and Franciskovic, 2010; Pietrzak et al., 2011). Paranoid traits are understandable as PTSD patients often feel a constant need to be vigilant and on guard. However, the reported proportions vary across studies, to which the present meta-analysis may provide more reliable estimates.

OCD-patients are chronic sufferers who experience major impairment especially related to physical/occupational and emotional functioning (Hollander et al., 1996; Hollander et al., 2010). The degree of any PD has varied from 66% (Stein et al., 1993) to as low as 4% (Joffe et al., 1988), with the OCD PD as the most frequent comorbid condition (Alnaes and Torgersen, 1988; Samuels et al., 2000; Skodol et al., 1995). Obviously, a comorbid OCD PD

may introduce a "double burden" in terms of intensified needs for order and perfection when performing OCD related checking or rituals in order to reduce anxiety.

From this brief outline of the literature, it is evident that a concurrent PD may impede both treatment and outcome of an AD, as well as possibly raising health care costs. The lack of previous meta-analyses covering all ADs, call for an empirical review to summarise and evaluate the current standing in the literature. It is also evident that the large between-study variation in the comorbid proportions of PDs across the various ADs, invite for a search for moderators that may explain this variability.

In the current study we examined the impact of diagnostic system (DSM-III-R versus DSM-IV), diagnostic methods (interview versus questionnaire), sample characteristics (patients receiving inpatient versus outpatient treatment), mean age of onset of AD and duration of AD. We expected higher comorbidity estimates from studies based on questionnaire data compared to structured interviews as that has been reported from PD comorbidity studies on for example eating disorders (Ramklint et al., 2010; Rosenvinge et al., 2000). Literature comparing the PD comorbidity between in- and outpatient samples is very scarce, except some findings indicating a higher degree of cluster B comorbidity in inpatients (Melartin et al., 2002). Hence, a clear-cut prediction could not be made, but the degree of comorbidity was expected higher among inpatients based on the psychiatric worse condition that an inpatient admission implies, particularly among patients with cluster B PDs. An early age of onset of an AD appears negative as it is associated with a longer duration of illness and a higher general symptom load in OCD (Wang et al., 2012), a history of childhood abuse a and worse clinical outcome in GAD (Goncalves and Byrne, 2012), as well as generally higher comorbidity with other ADs (Klein Hofmeijer-Sevink et al., 2012). Moreover, early onset has also been related to higher comorbidity estimates between OCD and OCD-PD (Coles et al., 2008), between GAD and any PD (Garyfallos et al., 1999), and between social phobia and

avoidant PD (Holt et al., 1992). Since the duration of an AD is partly related to the age of onset, we expected that an early age of onset and a longer duration of AD would imply a higher degree of comorbid PDs.

Hence, the paper had two primary aims: First, to compute mean weighted proportions of co-morbidity between the major axis I ADs and all axis II PDs. Second, to examine whether any of the moderators described above could explain the variability reported in the literature.

Method

Literature search

The current study was part of a larger meta-analytic project on the comorbidity between axis-I symptom disorders (depression, anxiety and eating disorders) and axis-II PD. The databases PsychINFO, Embase and Medline were searched for scientific papers on the comorbidity between anxiety and personality disorders published in the period between 1980 and 2010. The following keywords were used: “anxiety disorder" OR "anxiety disorders" OR phobia OR "panic disorder" OR "obsessive-compulsive disorder" OR "posttraumatic stress disorder" AND "personality disorder" OR "personality disorders" AND co-morbidity. The search yielded 1726 articles. By screening the abstract of the papers and excluding studies of patients recovered from an AD, or where the AD was comorbid to other axis-I diagnoses, the list was reduced to 71 papers. Additional 86 articles were located from the reference lists of 17 review papers that we identified (i.e., Baer et al., 1992; Bienvenu and Stein, 2003b; Eskildsen et al., 2010; Keeley et al., 2008; Marshall, 1996; Mavissakalian, 1990; McLaughlin and Mennin, 2005; Mennin and Heimberg, 2000; Merikangas and Angst, 1995; Ng and Bornstein, 2005; Papp et al., 1990; Pigott, 1998, 2003; Reich, 2009; Stein et al., 1993; Summerfeldt et al., 1998; Tillfors and Ekselius, 2009). As the present study was part of a larger meta-analytic project, 27 additional papers were found in addition to seven reviews (i.e., Dreessen and Arntz, 1998; Maser, 1998; Noyes, 2001; Reich, 2000, 2003; Ruegg and Frances, 1995; Vaglum, 2000), further extending the list with 59 papers. A total of 243 published articles were identified using these procedures.

Inclusion criteria

Empirical papers were eligible for inclusion in the meta-analysis if: (1) patients were > 18 years old, (2) the AD was the primary diagnosis, (3) information about the proportion of

comorbid PD was available, and (4) English or German language were used. Treatment studies were included if the proportion of PD was reported at baseline. Thus, 118 papers were excluded, yielding a final pool of 125 papers.

Coding procedure

From each study we coded general information about the article: author, year and country of publication, information about the sample (number of patients, proportion of women and mean age). Comorbid events of PD were entered as proportions. ADs were coded as panic disorder with (panic -a) or without agoraphobia (panic +a), social phobia, OCD, PTSD or GAD.

In accordance with the DSM-IV (APA, 1994), PD clusters were coded as: Cluster A (paranoid, schizoid and schizotypal PD), cluster B (antisocial, borderline, histrionic and narcissistic PD) and cluster C (avoidant, dependent and obsessive PD). If a PD diagnosis was based on the International Classification of Diseases (ICD, 1992), the equivalent DSM-IV diagnosis was used (e.g., anxious PD coded as avoidant PD, and emotional unstable PD as borderline PD). Proportions of any kind of PD (any PD), of the clusters A, B and C, and each of the specific PDs were coded.

As potential moderators, information about the mean age of onset of an AD, duration of the AD and duration of the PD (in years) was coded, as well as recruitment sample/type of patients (inpatients, outpatients, inpatients and outpatients, or primary care/community), gender distribution, diagnostic method for deciding an anxiety and a personality disorder (interview, questionnaire or a clinical assessment) and diagnostic system used (DSM: -III, -III-R, IV or -IV-TR, ICD: -9, -9-CM or -10). Information about blind scoring for AD and PD were also coded as yes, no or not reported.

Coding procedure

Two psychology students (Øvergård and Kaiser), trained by Rosenvinge and Friborg, coded the papers. The training included definitions and examples of the coding categories for all variables and an introduction to the data management process. Furthermore, for training purposes five randomly selected articles were independently coded by the raters and compared to the results of one supervisor. The number of disagreements was few, and if present, they were discussed with the supervisors until a consensus was reached. The inter-rater reliability was examined in a similar meta-analysis (Friborg et al., 2012) between the same student coder (Øvergård) and the first author (Friborg), and found highly satisfactory.

Statistics

The meta-analysis was conducted using the programme Comprehensive Meta-Analysis version 2.2.057 (released December 2010) (Borenstein et al., 2005a). SPSS v18.0 was used for other statistical analyses. The mean weighted event rate was estimated as proportions (number of PD cases/sample size), and used as effect sizes in the analyses. Calculations were based on a random effects model as the proportions may vary across studies due to other factors than random error, like illness severity or duration of an illness. Hence, variance in proportions may be partitioned in two sources: a) variance within studies (ε, random/sampling error), and b) variance between studies (θ, variance in true proportions) (Borenstein et al., 2005a; Hedges and Vevea, 1998). Each study was weighted by calculating the inverse of these variance components: $1 / (\varepsilon+\theta)$. Small studies imply a larger within-study variance component ($\varepsilon = \sigma^2/n$), thus lowering the weight given to data from small samples. A *Q* test statistic may be calculated to test whether the variance between studies is significantly different from zero, thus indicating that variation in proportions truly exists from which predictors (or moderators) may be sought. Furthermore, the random effects model reduces the type I error rate, hence enhancing the generalizability of the findings (Field, 2003; Lipsey and

Wilson, 2001). An analogous *Q*-test statistic for between-group differences may be conducted to examine whether the observed difference in proportions between two samples, divided by a categorical predictor (moderator), are significantly different. Continuous moderators were examined by conducting meta-regression analyses. The random effects slope parameter was estimated using the unrestricted maximum likelihood method (Borenstein et al., 2005b).

Results

Sample characteristics

Most studies were conducted in America (62 studies) and Europe (58 studies). Only seven studies came from other parts of the world. The five year publication rate was relatively steady with 19, 37, 22, 18 and 29 studies appearing within each period. The total number of patients in the 125 studies was 14 612. The study details are provided in Table 1. Most studies were conducted on outpatient samples (49%), while inpatient, a combination of inpatient/outpatient samples and recruited/community samples constituted 37%. Eighteen studies (14%) did not provide unambiguous information about sample type.

More women than men had panic disorders and GAD, while more men than women suffered from a PTSD. These numbers are not estimates of prevalence, but of the gender distribution in the clinical/recruited samples. For most ADs, the onset of illness was in the late twenties, except social phobia and OCD which debuted during the teenage years and the early twenties, respectively. Hence, the mean duration of illness was longer for these two disorders, in addition to GAD. PTSD, agoraphobia and OCD occurred most often in inpatients samples, while social phobia and panic disorder patients more often came from recruited samples.

The most common diagnostic system to diagnose an AD or a PD was the DSM-III/DSM-III-R (AD: 70.5% - PD: 73.4%), followed by the DSM-IV/IV-TR (AD: 27% - PD: 24.2%) and ICD-9/10 (AD: 2.4% - PD: 2.4%). The preferred assessment method for AD and

PD was a structured interview (AD: 82.5% - PD: 71.2%), followed by a subjective clinical assessment (AD: 13.5% - PD: 7.2%), questionnaires (AD: 1.6% - PD: 14.4%), and a combination of interview and questionnaires (AD: 2.4% - PD: 7.2%).

--- Table 1 ---

Comorbidity with personality disorder (PD) clusters

The comorbidity rate (mean proportion) of any PD (patients having at least one comorbid PD diagnosis) was high across all the subtypes of AD, ranging from .35 (PTSD) to .52 (OCD). As expected, the comorbidity rate of cluster C PDs combined across all ADs (.39) was significantly higher than cluster B PDs (.19) and cluster A PDs (.13) ($Q_2 = 86.5$, $p < .001$). The difference between cluster A and B PDs was significant ($Q = 4.62$, $p = .03$), but of small magnitude. The number of studies providing proportion estimates on the cluster level was however sparse, except for panic/agoraphobia and OCD showing a similar pattern across the cluster levels. A significant difference in the cluster C PD comorbidity was evident between panic disorders without (.22) and with agoraphobia (.38) ($Q = 5.23$, $p < .02$).

--- Table 2 ---

Comorbidity with specific PD

Of the estimates of comorbidity between a specific PD and the separate ADs (Table 3) social phobia had the highest rate of occurrence with the avoidant subtype (.46). Second came PTSD showing an elevated comorbid pattern across a number of specific PDs, notably paranoid, avoidant, borderline and OCD (range: .22-.26). All other specific PDs occurred at significantly lower rates (range: .03-.11). For the remaining ADs, panic disorders (with and without agoraphobia), GAD, OCD and AD-NOS, the level of cluster A and B specific PDs were generally low (range: .02-.11), while the cluster C specific PDs were observed more often (range: .08-.20). The avoidant and the OCD subtypes occurred more often than the dependent subtype. The comorbidity estimates in Table 3 were stable for most ADs as the

confidence intervals were small (generally within a window of 10%). PTSD on the other hand had wide confidence intervals, indicating a comorbidity of a considerable heterogeneous nature (e.g., ranging from .07 - .64 for the paranoid PD).

Moderators analyses

Due to a large number of possible moderator effects a selection was made for findings reporting (1) a significant heterogeneity statistic (Q_{within}), and (2) containing a minimum of three studies within each comparison group.

Sample (inpatients vs. outpatients): Among panic disorder patients, the proportion of an avoidant PD was higher among inpatients ($\overline{p}$ = .31, *k* = 3) than outpatients ($\overline{p}$ = .16, *k* = 17) (Q = 4.62, p < .05). This difference was opposite for narcissistic PD which was less frequent among inpatients ($\overline{p}$ = .01, *k* = 3) than outpatients ($\overline{p}$ = .09, *k* = 12) (Q = 8.90, p < .01). Among OCD anxiety patients, the proportion of an OCD PD was lowest among inpatients ($\overline{p}$ = .12, *k* = 3), higher among outpatients ($\overline{p}$ = .21, *k* =16), and highest among patients receiving both treatment types ($\overline{p}$ = .31, *k* = 3). Only the difference between inpatients and both treatment types was significant (Q = 3.94, p < .05). No other statistically significant differences emerged.

Diagnostic system: There was a trend toward lower proportions of a comorbid PD among patients with social phobia or OCD if diagnoses were based on the DSM-IV compared with -III/III-R (Table 4, first and second column). For panic disorders the patterns were more mixed. Cluster C OCD PDs occurred more often if the AD diagnosis was based on the DSM-III-R or the DSM-IV compared with the DSM-III. However, diagnoses of a PD based on the DSM-IV yielded lower comorbid estimates than diagnoses based on the DSM-III or the DSM-III-R.

Diagnostic method: AD diagnoses based on a clinical assessment yielded higher comorbid estimates within all PD clusters compared to a structured interview (Table 4, second last column). This tendency was in practice only evident for the OCD AD. The differences were largest within the schizotypal and the avoidant PDs. Questionnaire methods were rarely used to diagnose an AD. PD diagnoses based on questionnaires also yielded higher comorbid estimates than structured interviews (Table 4, last column). These differences were generally not large, except for cluster C PDs (notably the avoidant PD) among OCD anxiety patients. Data on clinical assessment were not suited for an empirical analysis.

Blind rating of AD and PD: As only two and seven studies provided positive and negative information about blinding, respectively, the effect of this moderator could not be analysed.

Meta-regressions examining continuous moderators

The following moderators were examined: Gender, mean age of onset and duration of an anxiety disorder. As the CMA program converts proportions to logits, an antilog calculation is necessary to provide a meaningful interpretation: $p = \frac{e^{\beta_0 + X_1\beta_1}}{1 + e^{\beta_0 + X_1\beta_1}}$.

Gender: This was reported as proportion of women participating in the studies. Sufficient data were only available for panic disorders, social phobia and obsessive-compulsive disorder. However, no meta-regression results were statistically significant.

Mean age of onset: An earlier mean age of onset of social phobia was related to a higher comorbidity of cluster C PDs, particularly an avoidant PD ($\beta_0 = 3.77$, $\beta_1 = -.227$, $p < .001$, $k = 16$), but also the dependent PD ($\beta_0 = 3.74$, $\beta_1 = -.377$, $p < .01$, $k = 9$). Calculating the comorbidity rate for 15, 18, 25 and 30 years of mean age using the above formula, revealed an avoidant PD comorbidity rate of 59.0%, 42.2%, 13.0% and 4.6%, and a dependent PD rate of 12.8%, 4.5%, 0.3% and 0.1%, respectively.

Duration of AD: Duration of illness only moderated the comorbidity between panic disorders and schizotypal PD (β_0 = -4.35, β_1 = .187, $p < .01$, $k = 11$), indicating a higher comorbidity the longer the duration of the panic disorder. The effect was however small, rising from 1.5% to 7.7% from 1 to 10 years.

Discussion

This present meta-analysis on the comorbidity of personality disorders (PD) in the major subtypes of anxiety disorders (AD), i.e., agoraphobia/panic disorder, generalised anxiety disorder (GAD), social phobia, post-traumatic stress disorder (PTSD), obsessive-compulsive (OCD) and unspecified AD was based on 125 studies. Most data were collected from outpatient samples. Overall, the risk of having at least one comorbid PD (any PD) was high across all subtypes, ranging from 35% in PTSD to 52% in OCD. On the cluster level, cluster C PDs (avoidant, dependent and obsessive-compulsive) were observed more than twice as often as cluster A (paranoid, schizoid, schizotypal, anti-social) or cluster B (borderline, histrionic, narcissistic) PDs. Within cluster C, the avoidant PD was the most frequent comorbid condition, followed by OCD and the dependent PD. These cluster level differences were only valid for panic disorders and OCD as the other AD studies provided less information about the PD cluster level comorbidity. As the cluster levels will not be retained in the DSM-5 due to weak empirical support (Sheets and Craighead, 2007), this is not relevant to address in future research.

As for the comorbidity of specific PDs, social phobia had the highest proportion of a an avoidant PD. For the remaining ADs, except PTSD, the comorbidity rates for the specific PDs were significantly lower. The heterogeneity statistics were generally significant across most subtypes of AD and PD. This indicates that the between study variance is a result of other factors than sampling error, and that moderators may be sought. However, as the

confidence intervals generally ranged within a window of 2-12%, except for PTSD and in a few other cases, the variance in PD comorbidity was considered too low to be of major clinical concern.

Compared to all other AD subtypes, patient groups suffering from PTSD had a highly different comorbidity profile with a mixture of PD comorbidity, mainly paranoid, avoidant, borderline and the OCD PD. The confidence intervals were large, but unfortunately, none of the moderators examined in the present study explained this variation. Clearly, PTSD stands out as clinically more heterogeneous in nature compared with the other ADs. This is in line with other research pointing out the considerable heterogeneous clinical picture characterizing this patient group (Suvak and Barrett, 2011). Moreover, the heterogeneity may be explained by the large variety in the nature and impact of traumatic exposures, and the fact that the issue of identifying core features of the disorder is still considered unresolved (Brewin et al., 2009). The present study thus confirms that the symptom overlap and heterogeneity often observed in PTSD involve a considerable mixture of personality traits and disorders. Interestingly, the paranoid PD was the most comorbid condition although it is suggested removed from the DSM-5. However, due the exceptionally high comorbidity variation of this PD compared with the other subtypes, and the lack of research on paranoid PDs in general (Skodol, 2012) that may substantiate this variation, its removal seems justified. The PD section in DSM-5 is meant to be frequently revised and as new revisions are issued it seems sensible to initiate continuous studies on whether this subtype may yield more substantial information.

Another noteworthy finding was that OCD AD patients did not have a noticeably higher occurrence of a comorbid OCD PD (.20) compared with the other cluster C PDs, notably the avoidant PD (.17). This may stand in contrast to several researchers claiming a particularly strong comorbid relation between OCD AD and OCD PD (Alnaes and Torgersen, 1988; Diaferia et al., 1997; Samuels et al., 2000). Nevertheless, the present estimate came

close to the proportion reported by Mancebo et al. (2005) in their review of all OCD AD-OCD PD studies between 1991 and 2004 (not higher than .25). The present estimate did not depend on the diagnostic system either (DSM-III-R versus DSM-IV), but it depended to some extent on the diagnostic methods used.

Structured interviews were by far the most often diagnostic method. Although the use of subjective clinical assessments and questionnaire methods were rare, they were used in varying degrees across the different AD subtypes and could hence bias the results. We examined this possibility by rerunning the analyses in Table 3 after first removing all studies using clinical assessments or questionnaires. We observed no noticeable differences from the original table as most comorbidity estimates dropped down systematically with only 1-3%. Hence, the inclusion of studies using clinical assessments or questionnaires methods did threat the validity of the findings, possibly due to the low number of studies and the use of a random effects model. The only noticeable exception to this pattern was the comorbidity between OCD AD and OCD PD which increased from .20 to .22, while OCD AD-avoidant PD dropped down from .17 to .14. Hence, the contention of a particular link between OCD AD and OCD PD made by others (Alnaes and Torgersen, 1988; Samuels et al., 2000; Skodol et al., 1995) was largely confirmed by the current study.

Moderator analyses

The use of different diagnostic systems did not influence the comorbidity estimates in a clear-cut manner, although PD diagnoses based on the DSM-IV system appear more conservative (lower proportions) than the previous DSM-versions. However, the magnitudes were low and should raise no concern for clinical practice. A consistent observation was that the DSM-system is widely used in studies of a European origin despite the fact that the ICD-system is their official diagnostic tool. This may be unfortunate as the failure to use this

system prevents across-system comparisons necessary for improvements and empirically based harmonization between the ICD and the DSM.

The use of structured interviews to diagnose a PD led to lower comorbidity estimates than the use of questionnaires. This was expected as several other meta-analyses have indicated a comparable pattern (Ramklint et al., 2010; Rosenvinge et al., 2000). This effect was however only evident for panic and OCD disorders, and not for GAD and social phobia. The difference was also more pronounced in the assessment of cluster A and B PD, but less of problem for cluster C PDs, which we have no explanation for. Structured interviews for diagnosing an AD also yielded a lower comorbidity than clinical assessments. This was only evident for the OCD AD, which might imply that a subjective clinical assessment of OCD ADs is particularly prone to over-diagnosing of axis II comorbidity. A tentative explanation may be connected to the claim that milder forms of autism spectrum disorders and neuropsychological deficits occur more often in OCD patients than in other AD diagnostic groups (Bejerot, 2007). Certain subtypes of OCD patients, such as hoarders, may stand out as particularly odd to clinicians (Samuels et al., 2007), which may contribute to the tendency to over-pathologise their unusual personality traits. This argument was partly supported by the present study as the schizotypal PD occurred more frequently among OCD patients than among agoraphobia, social phobia or GAD patients.

Of the continuous predictors, gender was not found to influence the comorbidity rates. Although a range of gender differences in axis I and axis II disorders are quite common (Tadic et al., 2009), gender differences in the degree of PD comorbidity did not receive support. Gender differences in the assessment of PD comorbidity may therefore be of less concern during clinical assessment.

An earlier age of onset of an axis I AD predicted an increased degree of PD comorbidity for social phobia only. The risk for developing a cluster C PD increased

markedly the earlier the patients developed a social phobia disorder. The high comorbidity observed in the present study was in line with numerous previous reports indicating a phenomenologically very close relationship between social phobia and the avoidant PD (Brooks et al., 1989; Reich, 2000; Rettew, 2000). A similar trend was also found for the development of a dependent PD, but the degree of comorbidity was quite small in comparison. The duration of the AD was examined, but almost all tests were non-significant or of a small effect. Hence, for the development of a comorbid PD an earlier age of onset of an AD appears to be much more important than the duration of an AD. This highlights the importance of early detection and treatment, and in particular of social phobia, to reduce the risk for the life-long chronic condition which this combination of disorders implies.

Implications for DSM-5

In the provisional drafts for the DSM-5, PTSD is proposed as part of a new cluster called "Trauma- and Stressor-Related Disorders" rather than being part of AD as in DSM-IV. Our findings support this revision due to the considerably larger heterogeneity in the PTSD comorbidity estimates compared with the other subtypes of AD in addition to the larger number of comorbid PDs. The clinical picture of PTSD is generally complex and shares a range of symptoms with both anxiety and depression disorders. The finding of a paranoid PD as a notable comorbid condition also adds weight, which may reflect the hypervigilance these patients often report to threat-related stimuli. Another reason for the observed heterogeneity in PTSD may be the multitude of stressors that may give rise to a trauma-related disorder, as each stressor or trauma may invoke a different pattern of memory intrusions and trauma-related symptoms, as well as different symptoms of anxiety, depression or grief.

Panic disorders in the DSM-IV is described as with or without agoraphobia, while the DSM-5 proposes to separate these into two separate diagnoses called "Panic Disorder" and "Agoraphobia". The present findings provide tentative support for this separation as the

frequency of cluster C PDs are significantly larger in panic disorder patients with agoraphobia than those not having agoraphobia (Table 2). The empirical support may however be less valid as it rests on a cluster model of PDs, which has poor validity (Sheets and Craighead, 2007). However, as the clinical severity of panic patients with agoraphobia appears more pronounced than in those without agoraphobia (Furakawa et al., 2009), and as the presence of a comorbid PD is considered highly influential for the natural course and treatment prognosis (Reich, 2003; Telch et al., 2011), the proposed separation converges with the present findings. Differences in phenomenology and clinical severity of panic disorders and agoraphobia should also be better accounted for in DSM-5 by the introduction of a dimensional assessment of personality function and pathological personality traits.

Four of the 10 PDs from DSM-IV are proposed removed from the DSM-5, i.e. the paranoid, schizoid, histrionic and dependent PDs (APA, 2010). Based on the current meta-analysis, removal of the schizoid PD should be the least controversial due to the very low prevalence across most AD subtypes in the present study, which also is the case in clinical samples in general (Skodol, 2012). The dependent PD is suggested removed due to low comorbidity in community samples, high variability in clinical samples and weak construct validity (Skodol, 2012). The present comorbidity estimates did not provide any clear-cut picture here, but the dependent PD had consistently lower comorbidity estimates than the avoidant PD. As avoidance behaviour is the prime behaviour that maintains an anxiety disorder, having an avoidant comorbid PD may represent a considerably poorer prognostic marker than a dependent PD. The additional benefit of assessing a comorbid dependent PD in patients with anxiety disorders may therefore be quite limited, especially among individuals with a social phobia.

A final note concerns the change in the way severity and complexity will be assessed in the DSM-5. In the DSM-IV, severity is not assessed separately, and hence, it is not possible

to indicate the degree of functional loss caused by a comorbid PD although the individual differences within a PD subtype may be large. All patients are assumed to suffer the same degree of functional loss. Due to this flaw, different types of PDs have become associated with better or worse prognostic indicators or outcomes, such as the schizotypal/borderline PDs (worse) compared with the avoidant/OCD PDs (better), without a systematic and consistent clinical procedure to support such associations (Skodol et al., 2002). The new approach in the DSM-5 of assessing degree of functional loss in terms of self and interpersonal functioning, in addition to the specific personality pathological traits, is an important step forward. Among other things, it should change the focus on certain PDs as more severe or disabling than others and acknowledge that any PDs may be potentially severe and complex depending on the degree of functional loss. Future studies may reveal whether the new diagnostic system will improve treatment of ADs and the predictive value of outcome relevant prognostic factors for these disorders.

Strengths and limitations

This is the first meta-analytic review encompassing all major subtypes of ADs, and where a large number of included studies made it possible to obtain stable comorbidity estimates. Publication bias is of less concern in studies of comorbidity than for example in clinical trials as any comorbidity estimate (either low or high) would be interesting. Hence, it is not possible to say what a negative result represents, thus reducing the problem of non-publications of negative results. Several funnel plots were examined, but none of them yielded skewed standard error distributions indicative of publication bias. Heterogeneity in the findings may also lead to an asymmetrical funnel plot. The combination of significant heterogeneity in the present study and lack of asymmetry thus makes publication bias highly unlikely.

In order to strengthen the validity of the comorbidity estimates, it was recorded from the papers whether blind rating of diagnoses had been employed or not. If studies using blind rating had provided similar comorbidity estimates as studies using standard diagnostic methods, that would have strengthened the validity of the estimates. These analyses were however not possible to conduct as too few studies provided data on blind rating. Future studies should therefore improve the methodology, or the research field could preferably settle on a standard way of assessing the validity of diagnostic ratings.

Conclusions

Do we need more studies on the comorbidity of axis-II PDs? Probably not due to rather small confidence intervals for panic disorder with agoraphobia, social phobia, GAD and OCD. However, the number of studies on pure panic disorders and PTSD are low. As PTSD also stand out as a very heterogeneous condition, future studies on comorbidity should focus on PTSD and the possible reasons for the considerable heterogeneity observed. On the other hand, future PD-comorbidity studies may be needed in view of the considerable changes in how PDs are conceived in the drafts for the forthcoming DSM-5. In particular, the new dimensional conception of personality traits and general level of functioning may provide new insights into the relation between social phobia and avoidant PD, as well as OCD and OCD PD. Nevertheless, our finding that a substantial proportion of AD patients also present with an avoidant PD should be addressed in the routine clinical assessment and treatment of AD patients.

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Table 1. *Overview of Study Characteristics Depending on Type of Anxiety Disorder*

AD	*N* $_K$	Women $_K$ %	Age $_K$	Onset $_K$	Duration $_K$	Sample type (%) In	Out	I&O	RC	X
All studies	14 612 $_{125}$	54 $_{92}$	35.8 $_{90}$	22.5 $_{56}$	11.5 $_{56}$	11	49	11	15	14
Panic –a	882 $_{17}$	63 $_{10}$	36.9 $_{9}$	27.7 $_{4}$	8.7 $_{3}$	0	24	19	28	29
Panic +a	3 303 $_{35}$	66 $_{29}$	35.8 $_{28}$	27.6 $_{20}$	7.5 $_{19}$	11	57	03	10	19
SP	2 122 $_{32}$	48 $_{26}$	34.1 $_{26}$	17.4 $_{17}$	15.9 $_{17}$	05	36	01	42	16
PTSD	2 357 $_{14}$	37 $_{12}$	39.7 $_{9}$	*na*	*na*	28	25	27	14	06
GAD	911 $_{16}$	67 $_{7}$	42.5 $_{7}$	28.9 $_{3}$	12.2 $_{3}$	04	62	04	20	10
OCD	3 075 $_{38}$	55 $_{31}$	34.0 $_{31}$	21.3 $_{24}$	12.1 $_{24}$	10	56	16	05	13
Healthy control	1 961 $_{17}$	57 $_{7}$	34.9 $_{8}$	25.4 $_{2}$	8.2 $_{2}$	04	75	06	03	12

Notes. Panic –a = Panic disorder without agoraphobia, Panic +a = Panic disorder with agoraphobia, SP = Social phobia, PTSD = Post-traumatic stress disorder, GAD = Generalised anxiety disorder, OCD = Obsessive-compulsive disorder, Other = Anxiety disorders not otherwise specified. *N* = Number of patients, *K* = Number of studies, *na* = not available data, In = Inpatient, Out = Outpatient, I&O = Both in- and outpatients, RC = Recruited/primary care/community samples, X = Unspecified.

Table 2. *Comorbid Proportions of Any and Clusters of Personality Disorders for Different Anxiety Disorders Based on a Random Effects Model*

	Any PD			Cluster A PD			Cluster B PD			Cluster C PD		
AD	*p*	$CI_{.95}$	N_K	*p*	$CI_{.95}$	N_K	*p*	$CI_{.95}$	N_K	*p*	$CI_{.95}$	N_K
All studies	.49	.45-.53***	10 582 $_{87}$	.13	.09-.18***	4 640 $_{30}$	.19	.15-.23***	5 139 $_{34}$	.39	.34-.44***	5 347 $_{35}$
Panic –a	.41	.33-.49***	608 $_{13}$	.14	.05-.32***	279 $_{4}$	.16	.09-.28***	317 $_{5}$	.22	.13-.34**	317 $_{5}$
Panic +a	.47	.40-.54***	2614 $_{30}$	.11	.08-.16***	1481 $_{14}$	.20	.15-.26***	1794 $_{18}$	.38	.31-.46***	1955 $_{19}$
SP	.48	.39-.56***	1190 $_{18}$	.09	.05-.15	322 $_{3}$	.06	.02-.21***	392 $_{4}$	.46	.36-.56*	391 $_{4}$
PTSD	.35	.21-.52***	1267 $_{7}$	.29	.04-.81***	199 $_{2}$	.27	.21-.33	199 $_{2}$	.63	.13-.96***	199 $_{2}$
GAD	.47	.39-.56***	864 $_{14}$	.07	.03-.16**	378 $_{4}$	.14	.08-.24**	378 $_{4}$	.36	.31-.40	378 $_{4}$
OCD	.52	.45-.59***	2117 $_{29}$	.13	.06-.24***	1122 $_{11}$	.15	.10-.22***	1201 $_{12}$	.34	.26-.42***	1249 $_{12}$
Other anxiety	.44	.35-.53***	1922 $_{16}$	.07	.01-.33***	859 $_{5}$	.10	.04-.23***	858 $_{5}$	.30	.21-.41***	858 $_{5}$
Healthy control	.15	.11-.21	625 $_{5}$	.03	.01-.09	566 $_{3}$	.03	.02-.05	565 $_{3}$	.12	.06-.21	565 $_{3}$

Notes. *p* = Mean weighted proportion of personality disorders, $CI_{.95}$ = 95% confidence interval. The Q_{within} test was used to test for heterogeneity in proportions an indicated as significant using asterix: * $p < .05$, ** $p < .01$ and *** $p < .001$. N_K = Total sample size (*N*) and number of studies ($_K$).

Table 3. *Comorbid Proportions of Specific Personality Disorders (PDs) for Different Anxiety Disorders Based on a Random Effects Model*

	PDs									
ADs	Paranoid	Schizoid	Schizotyp	Antisocial	Borderline	Histrionic	Narcissistic	Avoidant	Dependent	OCD
Panic –a	.06 [.03-.12*]	.04 [.01-.12***]	.04 [.02-.09*]	.04 [.02-.07]	.10 [.06-.18***]	.11 [.07-.17**]	.05 [.02-.09]	.15 [.11-.22***]	.13 [.07-.23***]	.09 [.06-.13*]
	439 $_{9}$	431 $_{8}$	514 $_{9}$	341 $_{6}$	515 $_{11}$	542 $_{11}$	486 $_{9}$	594 $_{11}$	528 $_{11}$	641 $_{11}$
Panic +a	.07 [.05-.10***]	.02 [.01-.05***]	.02 [.01-.04***]	.03 [.02-.05***]	.06 [.04-.10***]	.08 [.05-.11***]	.05 [.04-.08***]	.17 [.14-.21***]	.13 [.10-.18***]	.11 [.08-.15***]
	1955 $_{21}$	2001 $_{17}$	2000 $_{17}$	1813 $_{18}$	2426 $_{21}$	2612 $_{23}$	2320 $_{22}$	3045 $_{28}$	2747 $_{26}$	2694 $_{25}$
SP	.08 [.05-.12***]	.04 [.02-.08**]	.03 [.02-.07*]	.04 [.03-.07***]	.06 [.04-.09***]	.03 [.02-.05]	.03 [.02-.05]	.46 [.40-.52***]	.07 [.04-.11***]	.11 [.08-.14**]
	985 $_{16}$	908 $_{13}$	922 $_{14}$	523 $_{7}$	1044 $_{16}$	1016 $_{16}$	1006 $_{14}$	2032 $_{30}$	1166 $_{17}$	1068 $_{15}$
PTSD	.26 [.07-.64***]	.10 [.02-.33***]	.13 [.02-.51***]	.09 [.03-.24***]	.22 [.10-.41***]	.05 [.01-.19***]	.06 [.02-.20***]	.23 [.10-.46***]	.08 [.02-.24***]	.20 [.08-.41***]
	1076 $_{7}$	918 $_{6}$	918 $_{6}$	1672 $_{8}$	1401 $_{11}$	932 $_{7}$	932 $_{7}$	1076 $_{7}$	1076 $_{7}$	1076 $_{7}$
GAD	.05 [.04-.08]	.02 [.01-.03]	.04 [.02-.07*]	.03 [.01-.06]	.09 [.07-.13]	.08 [.05-.12*]	.04 [.02-.06]	.15 [.11-.21**]	.08 [.05-.11*]	.14 [.10-.18]
	545 $_{8}$	769 $_{10}$	732 $_{10}$	579 $_{8}$	741 $_{11}$	722 $_{10}$	687 $_{9}$	746 $_{11}$	783 $_{11}$	781 $_{11}$
OCD	.05 [.03-.09***]	.03 [.01-.06***]	.08 [.05-.11***]	.02 [.01-.04***]	.07 [.05-.10***]	.06 [.04-.10***]	.04 [.03-.07***]	.17 [.12-.23***]	.10 [.07-.14***]	.20 [.16-.25***]
	2130 $_{23}$	1932 $_{23}$	2398 $_{27}$	1819 $_{20}$	2198 $_{26}$	2116 $_{25}$	1857 $_{21}$	2059 $_{23}$	2187 $_{25}$	2658 $_{29}$
Other anxiety	.04 [.01-.13***]	.02 [.01-.06***]	.02 [.01-.07***]	.02 [.01-.04]	.06 [.03-.10***]	.05 [.02-.11***]	.02 [.01-.05]	.18 [.12-.25***]	.10 [.06-.17***]	.11 [.07-.17***]
	1566 $_{10}$	1665 $_{11}$	1217 $_{9}$	976 $_{9}$	976 $_{14}$	1222 $_{10}$	1215 $_{9}$	1564 $_{10}$	1659 $_{11}$	1659 $_{11}$
Healthy control	.02 [.01-.03]	.02 [.01-.08**]	.02 [.01-.06]	.01 [.00-.02]	.02 [.01-.03]	.03 [.02-.08]	.01 [.01-.03]	.03 [.01-.06]	.03 [.01-.07*]	.06 [.04-.10]
	668 $_{6}$	667 $_{6}$	669 $_{6}$	669 $_{6}$	668 $_{6}$	667 $_{6}$	650 $_{5}$	676 $_{7}$	674 $_{7}$	910 $_{8}$

Notes. Reported data (ex: .06[.03-.12**]) represent mean proportion of personality disorders, and in superscript, 95% confidence interval and the heterogeneity test statistic (Q_{within}) indicated as * $p < .05$, ** $p < .01$ and *** $p < .001$. Total sample size and number of studies [ex: 439 $_{9}$] are reported on the line below.

Table 4. *Statistically Significant Dichotomous Moderators of the Random Effects Comorbid Proportion Estimates for the Comorbidity between Personality Disorders (PDs) and Anxiety Disorders (ADs).*

ADs / PDs	Diagnostic system AD			Diagnostic system PD			Diagnostic method AD		Diagnostic method PD	
	[1] D3	[2] D3R	[3] D4	[1] D3	[2] D3R	[3] D4	I	CA	I	Q
Panic disorders [1]										
Cluster A PDs	.08 $_{3}$	.17 $_{9}$	.10 $_{5}$ $^{1<2**}$	*na*	.21 $_{6}$	.07 $_{3}$ $^{2>3***}$				
Paranoid				.04 $_{5}$	.09 $_{12}$	.06 $_{5}$ $^{1<2*}$				
Schizoid									.02 $_{17}$	.15 $_{4}$ ***
Schizotypal				.08 $_{5}$	.03 $_{10}$	.02 $_{3}$ $^{1>3**}$	.02 $_{20}$	.08 $_{3}$ ***	.02 $_{17}$	.10 $_{4}$ ***
Cluster B PDs	.15 $_{3}$	.20 $_{11}$	.21 $_{7}$ $^{1<3*}$							
Histrionic									.06 $_{22}$	.19 $_{5}$ ***
Avoidant									.16 $_{26}$	.25 $_{6}$ *
Dependent									.12 $_{26}$	.26 $_{5}$ *
OCD	.06 $_{7}$	.11 $_{19}$	.14 $_{7}$ $^{1<3**}$	.05 $_{6}$	.11 $_{16}$	.15 $_{5}$ $^{1<3**}$				
Social phobia									*na*	
Dependent	*na*	.12 $_{13}$	.02 $_{4}$ $^{2>3***}$	*na*	.09 $_{12}$	.03 $_{3}$ $^{2>3*}$				
GAD									*na*	
Any PD	.30 $_{3}$	.51 $_{8}$	**							
OCD										
Schizotypal							.06 $_{20}$	.22 $_{6}$ ***	.05 $_{20}$	.18 $_{5}$ **
Antisocial							.02 $_{14}$	.08 $_{5}$ ***		
Paranoid				.09 $_{5}$	.07 $_{10}$	.03 $_{6}$ $^{1>3*}$				
Borderline									.06 18	.15 $_{5}$ *
Histrionic				.12 $_{7}$	.07 $_{11}$	.03 $_{6}$ $^{1>3***}$	.05 $_{19}$	.13 $_{5}$ *		
Avoidant							.15 $_{18}$	.38 $_{4}$ *	.14 $_{18}$	.40 $_{4}$ *
Dependent	.14 $_{4}$	.12 $_{9}$	.06 $_{7}$ $^{1>3*}$	.19 $_{6}$	.11 $_{11}$	.07 $_{6}$ $^{1>3**}$	.08 $_{19}$	.21 $_{5}$ **	.08 $_{20}$	.26 $_{4}$ *

Notes. [1] Panic disorders with and without agoraphobia, D3 = DSM-III, D3R = DSM-III-R, D4 = DSM-IV, I = Interview, CA = Clinical Assessment and Q = Questionnaire. * $p < .05$, ** $p < .01$. *na* = not available data.