

The Co-Morbidity of Eating Disorders and Anxiety Disorders: A Review

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Objective: To critically review the literature examining the co-morbidity between eating disorders and anxiety disorders.

Method: A review of the literature on the co-morbidity between anorexia nervosa, bulimia nervosa and eating disorders not otherwise specified and the anxiety disorders of OCD, PTSD, social anxiety, GAD, panic and agoraphobia.

Results: Of the empirical studies undertaken, it is clear that anxiety disorders are significantly more frequent in subjects with eating disorders than the general community. Researchers have shown that often anxiety disorders pre-date eating disorders, leading to a suggestion that early onset anxiety may predispose individuals to developing an eating disorder. To date however, the research presents strikingly inconsistent findings, thus complicating our understanding of eating disorder and anxiety co-morbidity. Furthermore, despite indications that eating disorder prevalence amongst individuals presenting for anxiety treatment may be high, there is a distinct lack of research in this area.

Discussion: This review critically examines the available research to date on the co-morbidity of eating disorders and anxiety disorders. Some of the methodological limitations of previous research are presented, in order to highlight the issues which warrant further scientific investigation in this area. Copyright © 2007 John Wiley & Sons, Ltd and Eating Disorders Association.

Keywords: anorexia nervosa; bulimia nervosa; eating disorder not otherwise specified; OCD; social phobia; PTSD; panic disorder

INTRODUCTION

Research indicates that eating disorders and anxiety disorders frequently co-occur. Studies have consistently shown that a significant number of patients with anorexia nervosa (AN) or bulimia nervosa

(BN) experience one or more anxiety disorders (Kaye et al., 2004). The prevalence of anxiety disorders amongst BN samples has been reported in a number of investigations (Bulik et al., 2000; Brewerton et al., 1995; Hudson et al., 1983, 1987; Laessle et al., 1989; Piran et al., 1985; Powers et al., 1988; Schwalberg et al., 1992; Walsh et al., 1985). Similarly, prevalence amongst AN samples has also been investigated (Deep et al., 1995; Halmi et al., 1991; Herpertz-Dahlmann et al., 1996; Laessle et al., 1987) (see Table 1). Lifetime prevalence rates of at least one anxiety disorder varies from 25% (Keck

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Table 1. Lifetime and Current prevalence of anxiety disorders in patients with eating disorders

Reference & country	Subjects	N	Diagnostic criteria & instruments	Summary of results	Limitations of research
Brewerton et al. (1995) USA	BN	59	DSM-III-R; SCID	36% reported at least 1 AD 71% anxiety preceded BN	No specific ED diagnostic instrument; No control group
Bulik et al. (1996) New Zealand	BN	114	DSM-III-R; SCID; SCID II; SADS; HDRS; GAFS	64% reported at least 1 AD. AD had a mean onset of 8 year and BN mean age of onset 20 year	No specific ED diagnostic instrument; Sample not representative (exclusion criteria); No control group; Comorbid lifetime alcohol dependence in 48% of sample; No Ax PTSD
Bulik et al. (2000) USA	BN Monozyg twins	20 pairs	DSM-III-R; SCID	BN twin more likely to report lifetime GAD & mother report more anxious as child	Small sample size; No specific ED diagnostic instrument; No control group
Deep et al. (1995) USA	AN L/T recovered	24	DSM-III-R; SADS-L	75% prevalence of 1 AD 79% AD preceded ED	Small sample size; Sample not representative (exclusion criteria); No control group; No specific ED diagnostic instrument
Fornari et al. (1992) USA	AN BN	42 21	DSM-III-R; SADS-L	45.8% of AN had at least 1 lifetime AD	PTSD and SP not assessed; Small sample size; No specific ED diagnostic instrument; No control group; Males and females included
Godart et al. (2000) France	ANR BN	29 34	DSM-IV; DSM-III-R for AD; CIDI	72% AN-R at least 1 AD 65% BN at least 1 AD	Small sample size; No control group; No specific ED diagnostic instrument; Retrospective diagnosis; Males and females included
Godart et al. (2003) France	AN BN NC	166 105 271	DSM-IV; MINI	71% prevalence AD in ED 41.8–53.3% AD preceded ED	Sample may not be representative (more severe ED) Retrospective diagnosis; Small numbers in BN-NP group
Halmi et al. (1991) USA	AN NC	62 62	DSM-III-R; DIS; RDC-FH	62.9% at least 1 lifetime AD in AN 1 year prevalence in AN; OCD:11.3%; PD: 4.8%; Ph:24.2%	No specific ED diagnostic instrument; No Ax PTSD

Herpertz-Dahlmann et al. (1996)	Germany	AN adolescents	34	DSM-III-R; Morgan Russell SIAB-P; CIDI; BDI; ANIS; SCL-90 R	6 month prevalence: 41% at least 1 AD 53% reported AD preceding ED	Standardised measures not used at each time period; Small sample size and varying ages of sample; No control group; Males and females included
Hudson et al. (1983)	USA	AN BN AN + BN	16 49 25	DSM-III; DIS; EDS	54% ED group at least 1 AD	No specific ED diagnostic instrument; Inclusion of an AN + BN group; Small sample size and groups unequal
Hudson et al. (1987)	USA	BN Hx BN Depression NC	51 19 24 28	DSM-III; DIS; ADDS; EDS for ED	43% BN sample at least 1 AD	No specific ED diagnostic instrument; No Ax PTSD, SP and phobias; Apart from BN group, small sample; Males and females included
Iwasaki et al. (2000)	Japan	AN BN	98 73	DSM-IV; SCID-P	41% ED group at least 1 AD	Exclusion of EDNOS; No control group; No specific ED diagnostic instrument; Hospital sample more severe
Kaye et al. (2004)	USA	AN BN AN + BN	97 282 293	DSM-IV; SCID; YBOCS; STAI; FMPS; TCI	63.5% ED group at least 1 AD	Modified ED criteria; AD diagnosed when subthreshold EDNOS excluded; No control group; No specific ED diagnostic instrument; Query representativeness of sample
Keck et al. (1990)	USA	BN Bulimia DC NC	69 50 24 28	DSM-III-R; DSM-III; SCID	25% Prevalence of at least 1 AD in BN higher than NC though non sig	Sample not representative (exclusion criteria); No Ax of PTSD; No specific ED diagnostic instrument; Small control group
Laessle et al. (1989)	Germany	AN R ANBP BN BN-Hx AN	21 20 27 23	DSM-III; CIDI	33.3% At least 1 AD in AN-R 55% At least 1 AD in AN-BP 70.4% At least 1 AD BN 65.2% At least 1 AD BN-Hx AN	No Ax GAD & PTSD; No specific ED diagnostic instrument; Small sample size; No control group
Laessle et al. (1987)	Germany	AN AN + Bulimia BN DC	13 26 13 47	DSM-III; CIDI; EDI; EAT	23% prevalence of 1 AD in AN	Small sample size; No specific ED diagnostic instrument No Ax for PTSD & GAD; Males and females included

(Continues)

Table 1. (Continued)

Reference & country	Subjects	N	Diagnostic criteria & instruments	Summary of results	Limitations of research
Powers et al. (1988) USA	BN	30	DSM-III-R; SCID	53% At least 1 AD	No Ax PTSD; Small sample size; No specific ED diagnostic instrument
Schwalberg et al. (1992) USA	BN	20	DSM-III-R; AD/IS-R	75% prevalence of 1 AD 59.3% AD preceded ED	Small sample size; No control group; No specific ED diagnostic instrument

et al., 1990) to 75% (Schwalberg et al., 1992) in BN and from 23% (Laessle et al., 1987) to 75% (Deep et al., 1995) in AN.

Several studies have shown that, in most cases, the onset of an anxiety disorder precedes the onset of an eating disorder (Brewerton et al., 1995; Bulik, 2003; Deep et al., 1995; Godart et al., 2003; Schwalberg et al., 1992) (see Table 1 for summary). These findings have led some researchers to speculate that early onset anxiety disorders may represent a potential genetically mediated pathway toward the development of an eating disorder (Kaye et al., 2004), and at the very least it suggests that early onset anxiety disorders may in some way predispose individuals to the development of an eating disorder (Bulik et al., 1996).

Of the anxiety disorders, obsessive-compulsive disorder and social phobia have been found to have the highest co-morbidity with eating disorders. Table 2 provides a summary of the research findings investigating comorbid eating disorders and anxiety disorders. The prevalence rates of anxiety disorders also differs amongst the eating disorder subtypes a summary of which can be seen in Table 3 and Table 4 for AN and BN, respectively.

Whilst most studies have focused on the prevalence of anxiety disorders in eating disorder populations, significantly less research has examined the prevalence of eating disorders among anxiety patients (Bulik, 1995). As a result, there is a general lack of information as to frequency of eating disorder pathology among patients presenting to specialty anxiety clinics, and it is unclear whether eating disorders are more commonly associated with some anxiety disorders as compared to others (Black Becker et al., 2004). This raises the possibility that eating disorders may go unidentified and untreated, particularly given that eating disorder assessment and treatment is often viewed as a clinical specialty and subsequently many clinicians in anxiety clinics may not be adept at detecting eating disorder symptomatology (Black Becker et al., 2004). The only study we have found which investigates eating disorder rates amongst women presenting to an anxiety clinic is that by Black Becker et al. (2004). They found that 12% of 257 women presenting to an anxiety clinic met criteria for a possible eating disorder. Other studies have investigated eating disorder rates amongst specific anxiety disorders (Brewerton et al., 1993; Lipschitz et al., 1999) or amongst individuals with sexual abuse trauma (Pribor and Dinwiddie, 1992; Faravelli et al., 2004) and war veterans (Striegel-Moore et al., 1999).

Table 2. Summary of research papers investigating eating disorder comorbidity with anxiety disorders

Reference & country	Subject	N	Diagnostic criteria & instruments	Summary of results	Limitations of research
Fornari et al. (1992) USA	ANR ANBP BN	24 18 21	DSM-III-R; SADS-L	Lifetime OCD ANR (25%) and ANBP (66%) (sig difference). BN OCD (42.9%)	No Ax PTSD and SP; Small sample size; No specific ED diagnostic instrument; No control group; Males and females included
Gleaves et al. (1998) USA	AN BN EDNOS	121 103 70	DSM-III-R; BULIT-R; EAT; DES; TSC-40; TSC-40-ANX; PSS	AN: 47% PTSD/BN: 62% PTSD EDNOS: 74% reported traumatic event; 52% met criteria for PTSD	No control group; Type of trauma identified in less than 10% of sample Use of self report measure to diagnose PTSD
Godart et al. (2000) France	ANR BN	29 34	DSM-IV; DSM-III-R for AD CIDI	AN-R: SP55%; Ph34%; GAD24%; OCD21%; PD7%; AG3% BN: SP59%; OCD0%; GAD23%; AG6%; PDI5%; Ph21%	Small sample size; No control group; No specific ED diagnostic instrument Retrospective diagnostic procedure; Males and females included
Godart et al. (2003) France	AN BN NC	166 105 271	DSM-IV; MINI	AN GAD 45.6%; ANR: OCD 17.5%; ANBP OCD 21.8 BN GAD 31.4%	Sample may not be representative (severe ED); Retrospective diagnosis of past disorders; Small numbers in BN/ANP group
Hinrichson et al. (2003) UK	ANR ANBP BN NC	21 34 59 50	DSM-IV; BITE; DES-II; FNE	ANR: SP 71.4% ANBP: SP 88.2% BN: SP 67.8% NC: SP 30%	No specific ED and ANBP diagnostic instrument

(Continues)

Table 2. (Continued)

Reference & country	Subject	N	Diagnostic criteria & instruments	Summary of results	Limitations of research
Hudson et al. (1983) USA	AN BN AN + BN	16 49 25	DSM-III; DIS; EDS	AN: OCD69%; PD38%; AG13%; Ph25%; BN: PD39%; OCD24%; phobia12%; AG10% AN + BN: PD44%; OCD44%; AG24%; Ph4%;	No specific ED diagnostic instrument; Inclusion of an AN + BN group Small sample size and groups unequal; No Ax for SP
Iwasaki et al. (2000) Japan	ANR ANBP BNP BNNP	62 36 57 16	DSM-IV; SCID-P	In all subjects, OCD was most prev (19%); followed by SP (18%), PD (16%) and GAD (13%); 43% of sample met criteria for AD and lifetime prev GAD more prev amongst ANBP and BNP than ANR	Exclusion of EDNOS; No control group; No specific ED diagnostic instrument; Hospital sample may be more severe
Kaye et al. (2004) USA	AN BN AN + BN	97 282 293	DSM-IV; SCID; YBOCS; STAI; FMPS; TCI	Prevalence of OCD, PD, SP, AG and GAD did not differ significantly across ED subtypes OCD (35–44%); SP (16–23%); Ph (12–18%); GAD (8–13%); PD (9–11%); AG (2–4%); PTSD x3 more frequent in BN (13%) than AN (5%)	Modified ED criteria; AD diagnosed when subthreshold; EDNOS excluded No control group; No specific ED diagnostic instrument; Sample may not be not representative
Laessle et al. (1987) Germany	AN AN + BN BN DC	13 26 13 47	DSM-III; CIDI; EDI; EAT	AN: SP 23%; Ph: 15%; OCD 15%; AG 0% AN + BN: SP 50%; Ph: 19%; OCD 15% AG 15% BN: Ph: 46%; SP 31%; OCD 8% Ag 8%	Small sample size; No specific ED diagnostic instrument; No Ax for PTSD, GAD and PD
Laessle et al. (1989) Germany	ANR ANBP BN BN (Hx AN)	21 20 27 23	DSM-III; CIDI; EAT	ANR: SP 23.8%; Ph14.3%;OCD 9.5%; PD 4.8%; AG 0% ANBP: SP 40%; AG 20%; Ph 15%; OCD 10%; PD 5% BN: SP 48%; phob 37%; OCD 18.5%; AG 14.8%; PD 11% BN (Hx AN): SP 56.5%; AG 17.4%; OCD 13%; Ph 8.7%; PD 4.3%	No Ax for GAD & PTSD; No specific ED diagnostic instrument; Small sample size; No control group

Lilienfeld et al. (1998) USA	ANR: BN CW	26 47 44	DSM-III-R; SADS; KSADS Eating Disorder Family History Interview	ANR: OCD 62%; SP 31%; GAD 31%; Ph 27%; PTSD 7%; PD 4% BN: PTSD 30%; OCD 21%; Ph 19%; SP15%; GAD 13%; PD 4% CW: Ph 7%; PTSD 7%; SP 5%; OCD 5%; GAD 2%; PD 0% SP more frequent in ANR vs controls	No Ax for AG; Small AN sample; Unbalanced sample sizes
Milos et al. (2002) Switzerland	AN BN	84 153	DSM-IV; SCID-I	29% OCD in ED; no diff between AN and BN; Comorbid OCD assoc with longer hx of ED & earlier onset	Self-report retrospective data on ED course; No specific ED diagnostic instrument; No control group
Piran et al. (1985) Canada	AN BN	14 33	DSM-III; SADS; DST; BDI; MMPI; HSCL; HDS; HAS	Lifetime: AN: SP 53.8%; PD 42.8%; OCD 14%; AG 0%; Ph 0% BN: PD 52.7%; SP 48.7%; AG 3%; Ph 3%; OCD 0%	No Ax PTSD; No specific ED diagnostic instrument; No control group
Speranza et al. (2001) France	AN BN CW	58 31 89	DSM-IV; MINI; YBOCS	Current and lifetime prev of OCD sig higher ED (15.7% and 19%) than in general population (0% and 1.1%) AN current (19%) and lifetime (22.4%) BN current (9.7%) and lifetime (12.9%) ANBP higher prev than ANR and BN Anxiety preceded ED in 65% of cases	Small sample size of ED subtypes; AN inpatients vs BN outpatients may differ in severity of illness
Stiger & Zanko (1990) Canada	ANR ANBP BN NC PC	16 12 45 24 21	DSM-III-R; EAT; DSQ	30% of ED women report CSA. CSA more prevalent among BP group than ANR. Only 8% of NC reported trauma	Modified ED criteria; NC group may have been comprised of well functioning individuals (hospital staff etc) and therefore not representative of the normal population; small sample size; No specific ED diagnostic instrument

(Continues)

Table 2. (Continued)

Reference & country	Subject	N	Diagnostic criteria & instruments	Summary of results	Limitations of research
Thornton and Russell (1997) Australia	AN BN	35 33	DSM-III-R; CIDI; Personality Disorders Inventory	AN: 37% OCD BN: 3% OCD 21% of ED reported OCD; OCD usually predated ED 19% had premorbid OCDP	Inpatients only, therefore may be more severe and not representative of population; No specific ED diagnostic instrument; No control group
Turnbull et al. (1997) UK	AN BN EDNOS	90 54 20	ICD-10; DSM-III-R; SCID Childhood adversity and trauma interview	No differences between AN, BN and EDNOS groups: Lifetime and current rates of PTSD were 18% and 11% respectively. Comorbid PTSD was not associated with greater severity of illness.	The onset of PTSD in relation to ED not assessed; No specific ED diagnostic instrument No control group
Vize and Cooper (1995) UK	AN BN NC DC	40 60 40 40	DSM-III-R; interview based on EDE; SADS; PDQ-R; BDI; CECA	Sexual abuse of any form was identified in 52.5% of AN group, 35% of BN group and 12% of control group	Groups not equal in numbers; Results may underestimate sexual abuse given participants were only given one opportunity to disclose abuse

Table 3. Summary of research papers investigating AN and AD comorbidity

Reference & country	Subject	N	Diagnostic criteria & instruments	Summary of results	Limitations of research
Halimi et al. (1991) USA	AN NC	62 62	DSM-III-R; DIS; RDC-FH	AN: SP33.9%; OCD25.8%; AG14.5%; Ph12.9%; PD8.1% NC: Ph14.5%; PD8.1%; OCD6.5%; AG3.2%; SP3.2% Higher lifetime AG in AN vs NC	No specific ED diagnostic instrument; No Ax PTSD
Halimi et al. (2003) USA	ANR ANBP OCD	147 177 116	DSM-IV; SIAB; YBOCS	AN-R: 68% lifetime OCD AN-BP: 79.1% lifetime OCD	Modified criteria for AN; Sample may not be representative (family cases)
Herpertz-Dahlmann et al. (1996) Germany	AN adolescents	34	DSM-III-R; Morgan Russell; SIAB-P; CIDI; BDI; ANIS; SCL-90	SP21%; Ph17.6%; PD11.8%; AG5.9%; OCD0% 12% of sample had obsessive compulsive behaviour without meeting DSM-III criteria for OCD	Standardised measures not used at each time period; Small sample size and varying ages of sample; No control group; Males and females included
Matsumaga et al. (1999) Japan	ANR OCD	53 23	DSM-III-R; DSM-IV; MAS for AD; SDS; SCID-II; SCID-P	40% met criteria for OCD after excluding OC symptoms typical of ED; Comorbid OCD assoc with more severe ED symptoms	Small sample size; No specific ED diagnostic instrument
Pollice et al. (1997) USA	AN NC	48 18	DSM-III-R; HIRSD; BDI; HARS; STAI; YBOCS; YBOCS-ED	Anxiety and obsessionality most severe in underweight state, symptoms reduced after short term and long term weight restoration	Small sample; Mixed longitudinal and cross sectional design; No specific ED diagnostic instrument
Råstam et al. (1995) Sweden	AN NC	51 51	DSM-III-R; SCID-II	Sig more AN subjects (31%) met criteria for lifetime OCD compared with NC (8%). 20% of the AN group continued to meet OCD diagnosis at follow up compared with 6% of NC. Other than OCD there was No sig diff b/w AN and NC in AD prevalence	PTSD not assessed; No specific ED diagnostic instrument

Table 4. Summary of research papers investigating BN and AD comorbidity

Reference & country	Subject	N	Diagnostic criteria & instruments	Summary of results	Limitations of research
Brewerton et al. (1995) USA	BN	59	DSM-III-R; SCID	SP17%; GAD12%; PD10%; PTSD 3%; OCD3%	No specific ED diagnostic instrument No control group No Ax for AG
Bulik et al. (1996) New Zealand	BN	114	DSM-III-R; SCID; SCID II; SADS; HDRS; GAFS	Lifetime prevalence: SP: 30%; Ph: 30%; PD: 10%; OCD: 4%; AG without PD: 2%; GAD: 2%	No specific ED diagnostic instrument; Sample not representative (exclusion criteria); No control group; Comorbid lifetime alcohol dependence in 48% of sample; No Ax PTSD
Bulik et al. (2000) USA	BN Monozy twins	20 pairs	DSM-III-R; SCID	75% reported GAD prior to ED	Small sample size; No specific ED diagnostic instrument; No control group
Dansky et al. (1997) USA	BN CW	72 2929	DSM-IV	BN Current PTSD 21.4% BN Lifetime PTSD 36.9% CW Current PTSD 4.2% CW Lifetime PTSD 11.8% Sig difference b/w BN and CW	Telephone screening; No diagnostic instruments used for ED or AD
Hudson et al. (1987) USA	BN Hx BN	51 19	DSM-III; DIS; ADDS; EDS for ED	BN: OCD33%; PD/AG14% Hx BN: OCD32%; PD/AG26%	No specific ED diagnostic instrument; No Ax for PTSD, SP and phobias; Apart from BN group, small sample; Males and females included
Powers et al. (1988) USA	BN	30	DSM-III-R; SCID-P	Ph: 20%; SP: 17%; AG: 13%; GAD: 10%; OCD: 3%	No Ax for PTSD and PD; Small sample size; No specific ED diagnostic instrument
Rorty et al. (1994) USA	BN BN Hx NC	40 40 40	DSM-III-R; Proposed DSM-IV; SCID-P; SCID-II; EAT-SADS-L; EDQ; SAEQ; AEIII; PSY	No sig diff between BN group and NC in reported sexual abuse-BN (28.8%) v NC (20%) Non sexual abuse more prevalent in BN group vs NC	Sample may not be representative due to recruitment through advertisement; Problem associated with retrospective study-reliance on recollection
Schwalberg et al. (1992) USA	BN	20	DSM-III-R; ADIS-R	GAD: 55%; SP: 45%; OCD: 15%; Ph: 10%; PTSD: 10%; AG: 0%; PD: 0%;	Small sample size; No control group; No specific ED diagnostic instrument
Welch and Fairburn (1994) UK	BN NC PC	100 100 50	DSM-III-R; EDE; SCID	Sexual abuse reports were similar in BN groups vs control groups	Retrospective design; Interviewers not blind to the case status of subjects

A final point of interest in the area of eating disorder and anxiety comorbidity is whether a comorbid anxiety disorder has implications for the treatment and outcome of an eating disorder. It is clear that individuals with comorbid conditions often display more severe symptoms and subsequently may be at greater risk for a poorer treatment outcome. Research findings however, are inconsistent. Some studies have suggested that comorbid anxiety may be one indicator for poor outcome (Fichter and Quadflieg, 2004; Gleaves and Eberenz, 1994; Goodwin and Fitzgibbon, 2002; Halmi et al., 1973; Herpertz-Dahlmann et al., 1996; Procopio, Holm-Denoma, Gordon, & Joiner, 2006; Thompson-Brenner and Westen, 2005; von Ranson et al., 1999), however other studies have not found this to be the case (Bulik et al., 1996; Halmi et al., 1991 and Thiel et al., 1998) (A summary of these studies and their findings can be seen in Table 5).

Despite the significant number of research papers investigating the comorbidity between eating disorders and anxiety disorders, many are plagued by methodological problems, limiting the usefulness of findings (the limitations have been summarised in Tables 1–5). This paper aims to critically review the available literature examining the co-morbidity between eating disorders and anxiety disorders.

OBSESSIVE COMPULSIVE DISORDER (OCD)

A relationship between AN, BN and OCD has been suggested by clinical observation and, increasingly, by empirical investigation. A number of studies have reported significant comorbidity between individuals with eating disorders and OCD (Fornari et al., 1992; Godart et al., 2000; Halmi et al., 1991; Hudson et al., 1983, 1987; Iwasaki et al., 2000; Kaye et al., 2004; Laessle et al., 1989; Lilenfeld et al., 1998; Matsunaga et al., 1999; Milos et al., 2002; Råstam et al., 1995; Speranza et al., 2001; Thornton and Russell, 1997) (see Table 2 for summary). Thornton and Russell (1997) showed that OCD usually predated the onset of an eating disorder, suggesting that OCD may be a risk factor for developing an eating disorder. Milos et al. (2002) reported that individuals with OCD co-morbidity have a longer history of an eating disorder and are likely to have developed the eating disorder at an earlier age.

AN has a considerable overlap with obsessive-compulsive disorder (OCD) and this may reflect common neurobiological, genetic, or psychological

elements. Early descriptive studies suggested that 50%–100% of patients with AN showed obsessional or compulsive features. More recent studies have found a lower but still significant level of obsessions and compulsions among patients with AN (Halmi et al., 1991, 2003; Matsunaga et al., 1999; Pollice et al., 1997; Råstam et al., 1995) (see Table 3 for a summary of AN and OCD comorbidity findings). Fornari et al. (1992) and Speranza et al. (2001) found a significant difference in the OCD lifetime prevalence between purging AN and restrictive AN, where purging AN patients exhibited higher prevalence of OCD than the restricting AN patients.

There is some argument that the pattern of obsessions and compulsions most commonly present in AN is different from that found in OCD. Therefore, it is important to distinguish those behaviours that are not directly related to food, weight and shape. The lack of clear evidence regarding these mechanisms means that it is difficult to draw clear causal conclusions. However at a functional level, an important issue is that compulsive behaviours reduce anxiety levels. It can be hypothesized that the same function is served in the eating disorders, given the affect regulation function of restriction and bulimic behaviours (Lockwood et al., 2004). This however, does not explain the difference between the ego-dystonic nature of OCD and the ego-syntonic nature of eating disorders. This important distinction does need to be addressed.

Holden (1990) noted that the obsessions and compulsions of OCD patients are ego-dystonic whereas the preoccupations and rituals of AN patients are largely ego-syntonic. Mazure et al. (1994) suggested that phobic thoughts of food and weight repeatedly enter the mind of AN patients, but not necessarily against their will. Although these thoughts or preoccupations may be distressing, they are not regarded as senseless. This is in contrast to typical obsessions and compulsions unrelated to eating, which also may occur in AN patients (Bastiani et al., 1996).

One of the most common concerns raised in the current debate is whether people with AN display 'typical' or 'true' OCD symptoms as seen in patients diagnosed with primary OCD, or whether their symptoms are secondary to weight loss and malnutrition, or a combination of these. These concerns arise due to evidence that in conditions of semistarvation, psychologically 'normal' adults can develop a range of obsessional features. Keys et al. (1950) illustrated how obsessions and compulsions,

Table 5. Summary of research papers investigating treatment response and outcome of individuals with comorbid ED and AD

Reference & country	Subjects	N	Diagnostic criteria & instruments	Summary of results	Limitations of research
Bulik et al. (1996) New Zealand	BN	114	DSM-III-R; SCID; SADS-L; HRDS	Comorbid AD not associated with differences in BN symptoms. However, an AD was associated with a Hx AN and earlier age of onset of drug and alcohol dependence	No specific ED diagnostic instrument; Sample not representative (exclusion criteria); No control group; Comorbid lifetime alcohol dependence in 48% of sample; No Ax PTSD
Fichter and Quadflieg (2004) Germany	BN (Ax pre and post Tx and 2yr, 6yr and 12 yr F/U)	196	DSM-III; DSM-III-R; DSM-IV; SIAB-S; EDI; HSCL	Lifetime anxiety found in 36% & comorbidity was the strongest predictor of unfavourable outcome	Telephone interviews; Inpatients only therefore may be more severe; Retrospective assessment-bias; No control group
Gleaves and Eberenz (1994) USA	BN	464	DSM-III-R; self report questionnaire based on DSED-R	71% reporting a Hx of sexual abuse also had indicators of poor prognosis	Insufficient assessment of sexual abuse; possible underestimate of sexual abuse due to non disclosure; No control group
Goodwin and Fitzgibbon (2002) USA	AN or BN	28	EDI; BORI for SP	Individuals who did not enter treatment had significantly higher levels of social anxiety than those who engaged with treatment	Small sample size; The diagnostic criteria for ED and AD unclear; No specific ED or AD diagnostic instruments; No control group
Halmi et al. (1973) USA	AN	42	Feighner et al.	More severe non ED OC behaviours assoc with poor outcome. moderate to severe anxiety symptoms were frequent in those who did and did not recover	The diagnostic criteria for AD unclear; No specific ED or AD diagnostic instruments; No control group
Halmi et al. (1991) USA	AN (10 yr F/U) NC	62 62	DSM-III-R; DIS; RDC-FH	Recovered patients had the same prevalence of lifetime psychiatric dx as those with persisting ED symptoms	No specific ED diagnostic instrument; No Ax PTSD

Herpertz-Dahlmann et al. (1996) Germany	AN Outcome study Adolescents	34	DSM-III-R; Morgan Russell; SIAB-P; CIDJ; BDI; ANIS; SCL-90 R	41% at initial assessment met criteria for AD. At 7 years follow up 38% met criteria for AD Patients with poor outcome show higher levels of psychopathology	Standardised measures not used at each time period; Small sample size and varying; ages of sample; No control group; Males and females included
Pollice et al. (1997) USA	AN (underweight and at S/Trecovery) AN (at L/Trecovery) NC	22 26 18	DSM-III-R; HRSD; BDI; HARS; STAI; YBOCS; YBOCS-ED	Anxiety and obsessional most severe in underweight state, symptoms reduced after short term and long term weight restoration	Small sample; Mixed longitudinal and cross sectional design; No specific ED diagnostic instrument
Procopio et al. (2006) USA	Bulimic symptom Two Ax over 2.5 years	150	EDI; RSE; BDI; BAI	The level of anxiety symptoms significantly predicted the level of bulimic symptoms 2.5 years later	No specific ED or AD diagnostic instruments; Sample not classified as per DSM-IV BN criteria; No control group
Råstam et al. (1995) Sweden	AN NC	51 51	DSM-III-R; SCID-II; Morgan-Russell; EAT	20% of the An group continued to meet OCD diagnosis at follow up compared with 6% of NC	No Ax PTSD; No specific ED diagnostic instrument
Srinivasagam et al. (1995) USA	Recovered AN NC	20 16	EDI; FMPS	AN sample had higher perfectionism scores and greater symmetry and exactness scores than controls	Small sample size; Inclusion of women in recovery at least 1 year, therefore unclear whether some had longer recovery times which may impact on results
Thompson-Brenner and Westen (2005) USA	Bulimic Symptoms	145	DSM-IV; SWAP 200	Comorbidity was systematically related to treatment length and outcome, such that the comorbid patients tended to have longer and less successful treatments by clinician report.	Patients with and without DSM-IV BN included; Retrospective clinician reports; Different therapeutic approaches; Selective response rate-bias; No specific ED and AD diagnostic instruments; No control group

(Continues)

Table 5. (Continued)

Reference & country	Subjects	N	Diagnostic criteria & instruments	Summary of results	Limitations of research
Thiel et al. (1998) Germany	AN BN (Ax pre Tx and at 30 month F/U)	27 48	DSM-IV; YBOCS; EDI; Hamburg OCI	At assessment 37% met criteria for OCD; no sig diff between ED diagnosis and OCD status; Dropout was not related to OCD status; Poorer prognosis for BN and comorbid OCD; patients with most improved ED showed highest reduction in obsessions and compulsions	Significant drop out rate (19%); Small sample size; No specific ED diagnostic instruments; No control group
Toner et al. (1988) Canada	AN (14 year F/U) CW	47 26	Feigner et al. DSM III; DIS	Symptomatic and improved AN group were sig higher in AD than CW Symptomatic group had sig higher incidence of AD prior to onset of AN relative to asymptomatic group (83% vs 55% respectively)	No Ax PTSD and GAD; Retrospective recall in assessment of anxiety and depression
Von Ranson et al. (1999) USA	BN Recovered BN NC	31 29 19	DSM-III-R; SADS-L; YBOCS; HDRS; HARS; EDI	YBOCS scores for BN and recovered BN groups were similar and were significantly higher than NC group	OCD not diagnosed in BN group; Cross sectional design; Small sample size; No specific ED diagnostic instruments

Note: ED: Eating Disorder; AN: Anorexia Nervosa; ANR: Anorexia Nervosa Restricting type; ANBP: Anorexia Nervosa Binge Purge type; BN: Bulimia Nervosa; BNP: Bulimia Nervosa Purging type; BNINP: Bulimia Nervosa Non Purging type; EDNOS: Eating disorder not otherwise specified; AD: Anxiety Disorder; CW: Control Women; NC: Normal Controls; DC: Depressed Controls; PC: Psychiatric controls; SP: Social Phobia; GAD: Generalised Anxiety Disorder; OCD: Obsessive Compulsive Disorder; PTSD: Post Traumatic Stress Disorder; AG: Agoraphobia; Ph: phobia; PD: Panic Disorder; Hx: History of; Ax: Assessment; CSA: Child Sexual Assault; L/T: long term; S/T: short term; Tx: treatment; F/U: Follow up; b/w: between.

particularly those concerned with the preparation and consumption of food, develop under conditions of food restriction. This study also provides evidence for the possibility that the obsessive and compulsive symptoms observed in people with AN may at least partly be the result of their malnourished state, and not evidence of a true OCD. Some evidence for this comes from the discrepancy between inpatient and outpatient AN OCD rates, whereby lower rates have been reported in the latter group (Serpell et al., 2002).

Studies that have compared rates of OCD in AN and BN have usually found higher co-morbidity in AN. However, two Japanese studies found a significant number of BN participants met criteria for OCD (Iwasaki et al., 2000; Matsunaga et al., 1999), even after excluding the OCD-like symptoms typical of eating disorders. Matsunaga et al. (1999) also reported that BN subjects with concurrent OCD were more likely than subjects without OCD to have more severe mood and core eating disorder psychopathology. Among BN subjects with concurrent OCD, symptoms related to symmetry and order were most frequently identified, followed by contamination and aggressive obsessions, and checking and cleaning/washing compulsions (Matsunaga et al., 1999).

Perfectionism and Obsessive Compulsive Personality Disorder (OCPD)

As discussed above, the research into OCD and eating disorders reveals a significant relationship, and several researchers have reported that non food related obsessions and compulsions, including significantly more cleanliness, orderliness, perfectionism, rigidity, miserliness, scrupulosity have been identified in patients with eating disorders (Brumberg, 1988; Kasvikis et al., 1986; Rothenberg, 1986; Solyom et al., 1982). This has fuelled suggestions that distinct personality traits may be important in the development and maintenance of an eating disorder. The literature also suggests that perfectionism and dichotomous thinking may mediate the relationship between extreme concerns about shape and weight and rigid and intense dieting (Fairburn, 1997). Furthermore, Fairburn (1997) suggests that perfectionism and dichotomous thinking may mediate the relationship between intense, rigid dieting and binge eating. This has led to significant interest in investigating the prevalence of personality disorders in the eating disorders and subsequently, there have been a number of

structured investigations into Axis II diagnosis amongst eating disorder patients.

Gartner, Marcus, Halmi, and Loranger (1989) used the PDE to assess inpatient ED subjects and reported that 25.7% met diagnostic criteria for OCPD. None of the BN sample met criteria for OCPD leading to the speculation that this personality feature is more consistent with individuals with AN. However, Rossiter, Agras, Telch, and Schneider (1993) reported that 10% of their BN sample met criteria for OCPD. Thornton and Russell (1997) reported that 19% met criteria for comorbid OCPD, and this was almost exclusively found in the AN sample. Lilienfeld et al. (1998) reported that AN probands had higher rates of OCPD lending support to reports of perfectionism and inflexibility among individuals with restricting type AN. Lilienfeld et al. (1998) also found that 31% of AN probands met criteria for OCPD and OCD, leading to the suggestion that individuals with OCPD may be more vulnerable to the development of OCD than those without this personality pattern.

Social Phobia

Whilst the link between eating problems and obsessive-compulsive pathology has been clearly established (O'Brien and Vincent, 2003), other manifestations of fear, such as social phobia, agoraphobia and panic, have received less research attention (Hinrichson et al., 2004).

A number of studies show that social phobia is common in patients with eating disorders (Brewerton et al., 1995; Godart et al., 2000; Halmi et al., 1991; Hinrichson, Wright, Waller, & Meyer, 2003; Iwasaki et al., 2000; Kaye et al., 2004; Laessle et al., 1987, 1989; Lilienfeld et al., 1998; Piran et al., 1985; Powers et al., 1988; Schwalberg et al., 1992) (see Tables 2–4 for a summary of findings). Several studies suggest, that social anxiety may be a more common co-morbid condition with eating disorders than OCD, and some researchers have speculated that social anxiety may play a role in the aetiology of eating disorders (Black Becker et al., 2004).

Hinrichson et al. (2003) demonstrated that levels of social phobia in patients with AN and BN are significantly elevated compared to control women, and that social phobia is associated with higher levels of eating psychopathology in bulimic individuals.

The prevalence rate of social phobia and eating disorders has differed across studies. In AN, prevalence rates of between 16% (Kaye et al.,

2004) and 88.2% (Hinrichson et al., 2003) have been reported and between 17% (Brewerton et al., 1995; Powers et al., 1988) and 67.8% (Hinrichson et al., 2003) in BN. Lilienfeld et al. (1998) also reported that social phobia is significantly more frequent in AN than in controls. Two controlled follow-up studies of AN found differing results, one found a significantly higher rate of social phobia in AN than normal controls (Halmi et al., 1991), whilst the second found no difference (Råstam et al., 1995).

Agoraphobia

Studies investigating ED and agoraphobia have found varying results. In AN, lifetime prevalence of agoraphobia ranges from 0% (Laessle et al., 1989) to 3% (Godart et al., 2000) in restricting subgroups, whereas a study of binge/purge AN found a 20% rate (Laessle et al., 1989). In follow up studies of AN, significantly higher lifetime prevalence rates of agoraphobia have been reported in the AN group compared to controls (Halmi et al., 1991), however a study by Råstam et al. (1995) reported no difference.

The lifetime prevalence of agoraphobia in BN varies from 0% (Schwalberg et al., 1992) to 17.4% (Laessle et al., 1989). In the community, lifetime prevalence of agoraphobia in BN varies from 27% (Bushnell et al., 1994) to 34.5% (Garfinkel et al., 1995).

Panic Disorder

The findings of panic disorder co-morbidity amongst eating disorder samples is also varied with one study reporting between 9% and 11% prevalence (Kaye et al., 2004) and another finding between 42% and 52% prevalence (Piran et al., 1985). Bulimic samples have been varied, ranging from 0% (Schwalberg et al., 1992) to 39% (Hudson et al., 1983). Several studies have found the lifetime prevalence rates of panic disorder ranges from 4% (Lilienfeld et al., 1998) to 7% (Godart et al., 2000) in AN-R and is estimated to 15% in AN- B/P (Laessle et al., 1989). Two AN controlled outcome studies have estimated that the lifetime prevalence of panic disorder is 8.1%, and 6 month prevalence between 2% and 11.8% (Halmi et al., 1991; Råstam et al., 1995). Walters and Kendler (1995) reported that in a community study, individuals with 'possible anorexia' have the risk of panic disorder increased by 3.4.

Specific Phobia

The reported lifetime prevalence of specific phobias amongst individuals with eating disorders varies considerably, ranging from 0% (Piran et al., 1985) to 34% (Godart et al., 2000) in AN and from 10% (Schwalberg et al., 1992) to 46% (Laessle et al., 1987) in BN. Follow up studies have reported that there is no difference between AN and controls (Lilienfeld et al., 1998) however, in a community study, the risk for phobia is increased by 2 to 4 in AN subjects (Kendler et al., 1991; Walters and Kendler, 1995) and by 2.37 in BN subjects (Kendler et al., 1991).

Post Traumatic Stress Disorder (PTSD)

Although a history of trauma, particularly childhood sexual abuse, is considered to be a non-specific risk factor for the development of an eating disorder, surprisingly few studies have examined co-morbidity of PTSD with eating disorders (Black Becker et al., 2004). Studies investigating PTSD co-morbidity among eating disordered individuals have reported rates ranging from 11% to 52% (Gleaves et al., 1998; Turnbull et al., 1997). Faravelli et al. (2004) found that women who had been sexually assaulted were significantly more likely to report an eating disorder compared with women who had not been assaulted. This is supported by the literature reporting the most frequently reported psychiatric consequences of sexual abuse in women are PTSD, mood disorders, substance abuse disorders, eating disorders and sexual disorders (Putnam & Trickett, 1997; Dahl, 1989; Thompson et al., 2003).

A number of studies have demonstrated a positive association between child sexual assault (CSA) and clinical eating disorders (Johnson et al., 2002; Steiger & Zanko, 1990; Vize & Cooper, 1995; Welch & Fairburn, 1994). A meta-analysis by Smolak & Murnen (2002) found a relationship between CSA and eating disorders, such that CSA is associated with an increased likelihood of eating disorder symptomatology. Furthermore, Jacobi et al. (2004) reported that there was a high likelihood that sexual abuse preceded the eating disorder. However, there have also been a number of studies that have not found a relationship between CSA and eating disorders (Pribor & Dinwiddie, 1992; Rorty et al., 1994).

When considering the eating disorder subtypes, Dansky et al. (1997) reported current and lifetime rates of PTSD in women with BN to be high and

Mantero and Crippa (2002) reported that PTSD subjects were considered to be at 3.36 times the risk of developing BN. Tozzi et al. (2003) report that several studies have shown that psychological stress or stressful life events can trigger the onset of AN. However, the nature and identity of these stressors remain poorly defined (Beumont et al., 1978; Casper & Jabine, 1986; Pyle, Mitchell, & Eckert, 1981; Strober, 1984). Kaye et al. (2004) observed that PTSD was approximately three times more frequent in individuals with BN as opposed to those with AN.

Generalised Anxiety Disorders (GAD)

Considerably less research has considered the relationship between eating disorders and GAD, however Godart et al. (2000) and Lilenfeld et al. (1998) estimate the lifetime prevalence of GAD in AN to be 31% and 24%, respectively. Studies reviewing the relationship between GAD and BN have found that lifetime prevalence varies between 10% (Powers et al., 1988) and 55% (Schwalberg et al., 1992). Kaye et al. (2004) identified GAD in their AN and BN sample of 13% and 7%, respectively, which is significantly lower than the 45.6% and 31.4%, respectively, reported by Godart et al. (2003). Iwasaki et al. (2000) reported that 13% of their AN and BN subjects met the criteria for GAD, and interestingly, their findings indicate that GAD was more prevalent amongst the purging subtypes of both AN and BN subjects, although this difference did not reach significance.

Bulik et al. (2000) reported that the maternal perception of greater childhood anxiety was supported by the twin self report, with the affected twin being at a greater risk for lifetime GAD. They suggested that because the age of onset for GAD was reported to be prior to or concurrent with the onset of BN in 75% of the cases, it is possible that the anxiety may be a predisposing factor rather than a sequelae of BN. These results support a growing body of literature that has reported elevated rates of premorbid anxiety disorders in women with BN (Bulik et al., 1997; Deep et al., 1995).

Eating Disorders Amongst Individuals With Anxiety Disorders

There is less research available examining the prevalence of eating disorders amongst individuals with anxiety disorders. Of the studies that have considered this, they have generally examined rates

of eating disorders concurrent with one particular anxiety disorder, usually OCD (Bulik, 1995). Among female OCD patients, eating disorder co-morbidity estimates have ranged from 11% to 42% depending on the type of eating disorder and the method of assessment (Bulik, 1995). Brewerton et al. (1993) reported that 20% of women with social phobia met the criteria for an eating disorder. Lipschitz et al. (1999) reported that 25% of an adolescent mixed-gender PTSD inpatients met the criteria for an eating disorder. Black Becker et al. (2004) indicates that although the number of studies is limited, estimates of the prevalence of eating disorders amongst anxiety disorder patients is high. Reported rates are markedly higher than the estimated prevalence of AN or BN among young females.

LIMITATIONS IN THE RESEARCH

Many studies investigating the co-morbidity between eating and anxiety disorder suffer from general methodological limitations (Mitchell et al., 1991; Schwalberg et al., 1992; Godart et al., 2002; Micali and Heyman, 2006; Godart et al., 2006). The variability between estimated co-morbidity of anxiety disorders and eating disorders amongst the available research is a significant limitation when considering the prevalence of co-morbid disorders. A number of factors may contribute to this variability.

Sample Sources and Selection

Research into ED and AD often include samples from various sources including inpatients, outpatients and community samples. Unfortunately this may bias the sample, as one could expect that an inpatient sample may be more likely to have multiple diagnoses and may not be representative of all patients with the disorder (Godart et al., 2002). Furthermore, some researchers have used exclusion criteria that may limit the frequency of comorbid AD. Keck et al. (1990) excluded all subjects with comorbid substance abuse, despite patients with AD often reporting comorbid substance abuse (Bulik et al., 1996). Several studies excluded subjects taking psychoactive medication (Bulik et al., 1996; Bulik et al., 1997; Deep et al., 1995; Keck et al., 1990) and subsequently may have diminished the rates of AD identified.

General Methodological Limitations

General methodological limitations included: (1) In many of the studies reviewed in this paper, the sample sizes were small, often including at least one group of less than 30 subjects; (2) Some studies include both males and females, while it is recognised that women have more lifetime AD than men (Wittchen and Essau, 1993) and that ED are rare in men (Godart et al., 2002); (3) Few studies are controlled, and often those that are controlled have larger control groups than ED groups and are not matched for age or other characteristics; (4) The definition of current prevalence varies across studies, referring to either 6-month (Herpertz-Dahlmann et al., 1996; Råstam et al., 1995) or 1-year prevalence (Halmi et al., 1991).

Diagnostic Criteria for Eating Disorders and Anxiety Disorders

Changes in diagnostic criteria for ED and AD over the past 15 years [e.g. Feighner criteria (1972), Research Diagnostic Criteria (RDC) (1977), DSM-III (APA, 1980), DSM-III-R (APA, 1987), DSM-IV (APA, 1994)] have clearly had an impact on the prevalence findings. Even in more recent studies, it is sometimes unclear whether they have utilised the DSM-IV or ICD-10 criteria to diagnose ED (e.g. Goodwin and Fitzgibbon, 2002). Changes in AD diagnostic criteria may also have impacted on the findings of studies over time. For example In the RDC (1977) and the DSM-III (1980) it was not possible to diagnose a depressive disorder and AD simultaneously, which may have influenced the prevalence of AD reported in some studies (Godart et al., 2002). It is possible that certain anxiety disorders may have been over reported due to the changes in diagnostic criteria between the DSM-III and the DSM-III-R. Specifically OCD and Social phobia DSM-III-R criteria stipulates both disorders cannot be diagnosed if the obsessions and compulsions or the social anxiety are exclusive to food related concerns. Whilst some researchers already incorporated this in addition to DSM-III criteria it may provide an explanation as to higher rates of both of these disorders in earlier studies. Finally, the number of anxiety disorders assessed often differs between the studies and will obviously affect the prevalence rates. A number of the studies reported in this paper excluded certain AD from the assessment, which is a significant limitation when drawing conclusions about prevalence rates of AD and ED. Significantly, it is not uncommon in the

research to exclude PTSD from the anxiety assessment, and this presents a limitation when considering the suggestion that a history of trauma, particularly CSA is a non-specific risk factor for the development of an eating disorder (Black Becker et al., 2004).

Diagnostic Instruments

Diagnostic instruments used to assess both eating disorders and anxiety disorders have also varied across studies and present a significant limitation when drawing conclusions about ED and AD comorbidity (Micali and Heyman, 2006; Godart et al., 2006). Unfortunately, many of the studies presented in this paper have failed to use well-standardised, internationally accepted diagnostic instruments to identify eating disorders, limiting the usefulness of their findings. Similarly, some of the research has used inadequate diagnostic instruments or criteria to identify anxiety disorders. This is particularly important to enable one to distinguish between eating disorder and anxiety symptomatology. For example considering the high but also variable rates of reported OCD in eating disorder populations, one may conclude that some research has insufficiently distinguished between obsessive compulsive symptoms that are secondary to malnutrition and the ED and those which may reflect a true OCD. Furthermore, as mentioned by Bulik et al. (1996), GAD in the SCID (with DSM-III-R criteria) is skipped for subjects with a current mood disorder. A number of the studies reported in this paper have used the SCID (e.g. Brewerton et al., 1995; Bulik et al., 1997; Powers et al., 1988; Råstam et al., 1995; Walters and Kendler, 1995) and therefore the rates of GAD may be an underestimate in these studies.

SUMMARY AND RESEARCH IMPLICATIONS

It is clear from the research that anxiety disorders are significantly more frequent in subjects with eating disorders than the general community. The available research investigating the prevalence of anxiety disorders amongst eating disordered individuals presents strikingly inconsistent findings. Whilst there are a large number of studies researching this area, the inconsistencies complicate the understanding of eating disorder and anxiety comorbidity. This presents the need for researchers to use well-standardised, internationally accepted instruments to identify and investigate both eating disorders

and anxiety disorders. Furthermore, the lack of research into the prevalence of eating disorders amongst individuals presenting for anxiety treatment, despite indications that prevalence may be high, suggests the need for greater research in this area.

A study currently being undertaken by the authors endeavours to examine the comorbidity between eating disorders and anxiety disorders using well standardised, internationally accepted diagnostic instruments and questionnaires. The current literature would suggest that further investigation into the co-morbidity between anxiety and eating disorders may have significant aetiological and therapeutic implications.

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