ENVIRONMENTAL RISK FACTORS AND THERAPEUTICAL IMPLICATIONS IN EATING DISORDERS

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„Man sieht nur mit dem Herzen gut.
Das Wesentliche ist für die Augen unsichtbar.“

Antoine de Saint-Exupéry

Für Ino, Hermann, Albert, Luis und Claudia:

„Ich kann die einfachste praktische Aufgabe nur mittels großer sentimentaler Szenen bewältigen. Wenn ich nach rechts gehen will, gehe ich zunächst nach links und strebe dann wehmutig nach rechts. Der Hauptgrund mag Angst sein: nach links zu gehen muss ich mich nicht fürchten denn dorthin will ich ja eigentlich gar nicht.“

Franz Kafka 14. Mai 1916

Dank euch habe ich es geschafft doch noch nach rechts zu gehen.

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LIST OF ABBREVATIONS

AAP = American Academy of Pediatrics

ABA = Activity-Based Anorexia Nervosa

ADA = American Dietetic Association

AN = Anorexia Nervosa

APA = American Psychiatric Association

AN-BP = Anorexia Binge-Purging Subtype

AN-CROSS = Anorexia Nervosa who cross over to Bulimia Nervosa

ANIS = Anorexia Nervosa Inventory Scale

AN-R = Anorexia Nervosa restrictive subtype

AN-BP = Anorexia Nervosa binge/purging subtype

BED = Binge Eating Disorder

BN = Bulimia Nervosa

BCDS = Bulimic Cognitive Distortions Scale

BDNF = Brain Derived Neurotrophic Factor

CAT = Cognitive Analytic Therapy

CBT = Cognitive Behaviour Therapy

CCQ = Cross Cultural (Environmental) Questionnaire

CR = Conditioned Response

CS = Conditioned Stimulus

DAA = Dieteticians Association of Australia

DSM-IV = Diagnostic and Statistical Manual of Mental Disorders

DU= Drug Use

EAT = Eating Attitudes Test

EDs = Eating Disorders

EDE-S = Eating Disorders Examination-Screening Version

EDI = Eating Disorder Inventory

EDNOS = Eating Disorders Not Otherwise Specified
ERP = Exposure with Response Prevention
HD = High Density
ICD = Impulse Control Disorder
IF = Global Impact Factor
LD = Low Density
MC4R = Melanocortin 4 Receptor
MDD = Major Depressive Disorder
NICE = National Institute of Clinical Excellence
OCD = Obsessive Compulsive Disorder
RANZCP = Royal Australian and New Zealand College of Psychiatrists
SAM = The Society for Adolescent Medicine
SNRIS = Serotonin-Norepinephrine Reuptake Inhibitors
SSRIS = Selective Serotonin Reuptake Inhibitors
STAXI-2= State Trait Anger Inventory-2
SU = Substance Use
SUD = Substance Use Disorder
TCA = Trastorno de la Conducta Alimentaria
US = Unconditioned Stimulus
UR = Unconditioned Response
YSR = Youth Self-Report Inventory

PREFACE

This dissertation, presented to obtain the degree of Doctor by the University of Barcelona, is the result of 9 studies carried out during a 4-year period at the Eating Disorder Unit (Department of Psychiatry) of the University Hospital of Bellvitge and the Department of Personality, Evaluation and Treatment at the University of Barcelona. The following articles have been published in international journals, as a result of the work performed, with a global impact factor (IF) of **15,609** (ISI-knowledge, JRC 2007) for the papers used for the present thesis and an IF of 21,843 for all the papers in which I collaborated.

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[http://www.uv.es/psicologica/ paper accpeted 26 th of May 2008.

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Calero, A., **Krug, I.,** Davis, K., Lopez, C., Fernández-Aranda, F., & Treasure, J. (Submitted). Meta-Analysis on drugs in people with eating disorders.

Studies where I collaborated but which will NOT be included in the thesis.

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1. INTRODUCTION

Eating Disorders (EDs) are among the most frequent chronic psychiatric illnesses of adolescence and young adulthood leading to severe physical and psychological health consequences for the sufferer and the family (Mond, Hay, Rodgers, Owen, & Beumont, 2005; Patton, Coffey, & Sawyer, 2003). Anorexia nervosa (AN) has the highest mortality rate of any psychiatric disorder (Birmingham, Su, Hlynsky, Goldner, & Gao, 2005). The fatal financial and social impact of these lethal illnesses on productivity, disability and quality of life remains unknown (Simon, Schmidt, & Pilling, 2005).

Eating disorders have multifactorial causes (Jacobi, Hayward, de Zwaan, Kraemer, & Agras, 2004), where environmental and biological-genetic factors are continuously involved. Notwithstanding the fact that approximately half of the contributing factors of EDs are non-genetic in origin, environmental causes have hardly been examined. Research has mainly centred on the discovery of new genetic and physiological causes and has neglected a cross-cultural standpoint. In addition, the literature on the aetiology of EDs has been troubled by the fact that the minority of studies meet the thorough quality criteria, as regards to methodology and sample sizes. Therefore according to an outstanding contemporary systematic review on EDs "replication studies are needed" (Stice, 2002).

Until the present moment the progress of efficient prevention and treatment approaches has been held back by the obscure knowledge of the aetiology of EDs. Even though behavioural interventions have been revealed to be successful especially in bulimia nervosa (BN) and to some extent also in binge eating disorder (BED), interventions in anorexia nervosa (AN) and eating disorders not otherwise specified (EDNOS) have inadequately been assessed (Simon et al., 2005). In Europe and across the world numerous countries are putting all their efforts together to develop guidelines for the management of EDs [e.g. National Institute for Clinical Excellence (NICE) (www.nice.org.uk), Dieticians

Association of Australia (DAA) (http://www.daa.asn.au/)]. However evidence based research for these guidelines still needs to be implemented and reinforced.

The present thesis entails new research intended at generating an integrated etiological model of EDs. We will undertake mixed basic and psychological research across different types of EDs (AN, BN, BED and EDNOS) and across different European countries, to detect shared and distinctive factors associated with EDs. In addition we will test certain therapeutical interventions for various forms of ED subtypes. We anticipate that the findings from the current dissertation will lead to an improvement in the current body of knowledge of EDs.

2. EPIDEMIOLOGY

2.1. Epidemiology of eating disorders in Western countries

Eating disorders affect approximately 2-5% of the female population in Western countries (Hudson, Hiripi, Pope, & Kessler, 2006; Wittchen & Jacobi, 2005). Likewise, in Spain, various population-based studies (e.g., (Olesti Baiges, Pinol Morese, Martin Vergara, de la Fuente Garcia, Riera Sole, Bofarull Bosch et al., 2008; Pelaez Fernandez, Labrador, & Raich, 2007; Rodriguez-Cano, Beato-Fernandez, & Belmonte-Llario, 2005; Sepulveda, Carrobles, & Gandarillas, 2008) have revealed prevalence rates ranging from 1% to 3.5%.

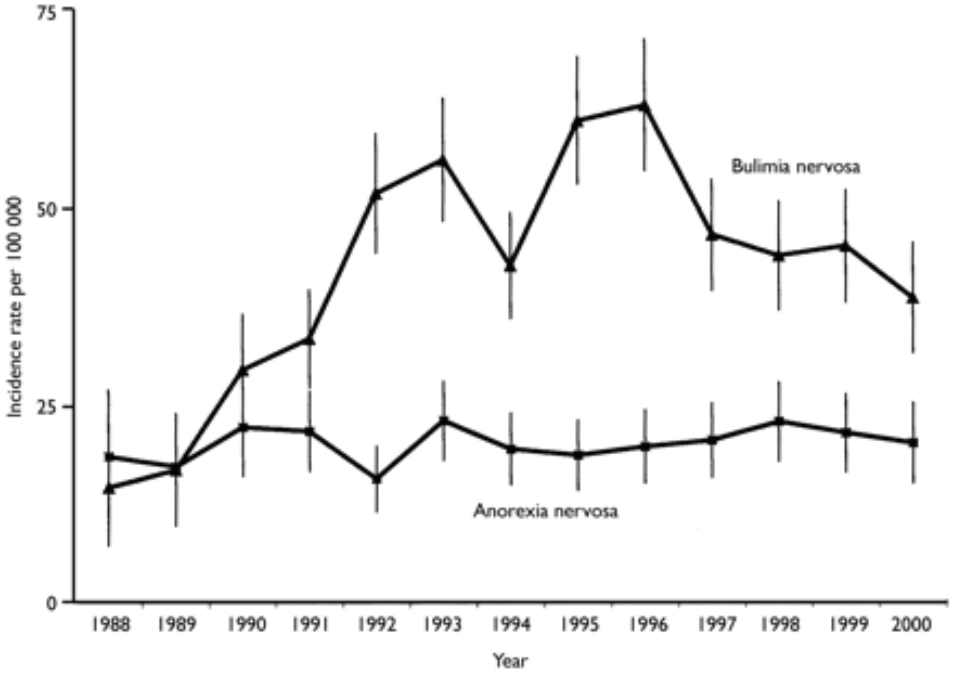
Two recent systematic reviews on the prevalence of EDs indicate a mean prevalence rate of 0.3 % for AN and values varying from 0.37% to 1.3% for subthreshold AN (Hoek, 2006; Hoek & van Hoeken, 2003). Research on the changing incidence of AN has been conflicting, with some studies (Hoek, 2006; Milos, Spindler, & Schnyder, 2004) suggesting an increase of AN and others documenting steady rates (Currin, Schmidt, Treasure, & Jick, 2005; Inagaki et al., 2002).

As regards to BN a prevalence rate of 1.5% for threshold BN and 5.4% for subthreshold BN has been reported (Hoek, 2006; Hoek & van Hoeken, 2003). A recent ED epidemiological study has suggested a decrease in the prevalence of BN during the last 20 years (Keel, Heatherton, Dorer, Joiner, & Zalta, 2006). However, since BN is a relatively new disorder not much is known about its changing incidence. *Figure 1* illustrates the changes in the incident rates for AN and BN from 1988 to 2000.

Little is known about the distribution of EDNOS even though it is the most common ED diagnosis. This could partially be attributable to the fact that there has been no simple definition of what constitutes an

atypical ED. A recent study on the occurrence of EDNOS in the general population has found a prevalence rate of 2.37% (Machado, Machado, Goncalves, & Hoek, 2007) and another previous study documented a lifetime rate of atypical EDs of 4.7% (Favaro, Ferrara, & Santonastaso, 2003).

Figure 1: *Incidence Rate for Anorexia Nervosa and Bulimia Nervosa from 1998 to 2000 (Currin et al., 2005)*



As regards to BED, population-based studies have indicated prevalence rates ranging from 0.7% to 3.0% for full BED (Striegel-Moore & Franko, 2003) and values from 5% to 8% for obese individuals (Bruce & Wilfley, 1996). A detailed summary of the prevalence estimates for each ED subdiagnosis can be found in *table 1*.

2.2. Problems associated with the epidemiological research on eating disorders

It should be noted that determining the exact occurrence of EDs is problematic, as some sufferers may assertively avoid detection and present themselves to medical specialties under a variety of different diagnostic guises (Ghaderi & Scott, 1999; Hoek, 2006). Moreover, the indexes for ED diagnoses should be considered carefully, since accurate diagnosis of EDs has long been problematic due to the difficulty of detecting sub-clinical cases and the lack of straightforward wide-spectrum assessment tools (Dalle Grave & Calugi, 2007).

Table 1: *Review of the Prevalence of Anorexia Nervosa and Bulimia Nervosa (Hoek & van Hoeken. 2003)*

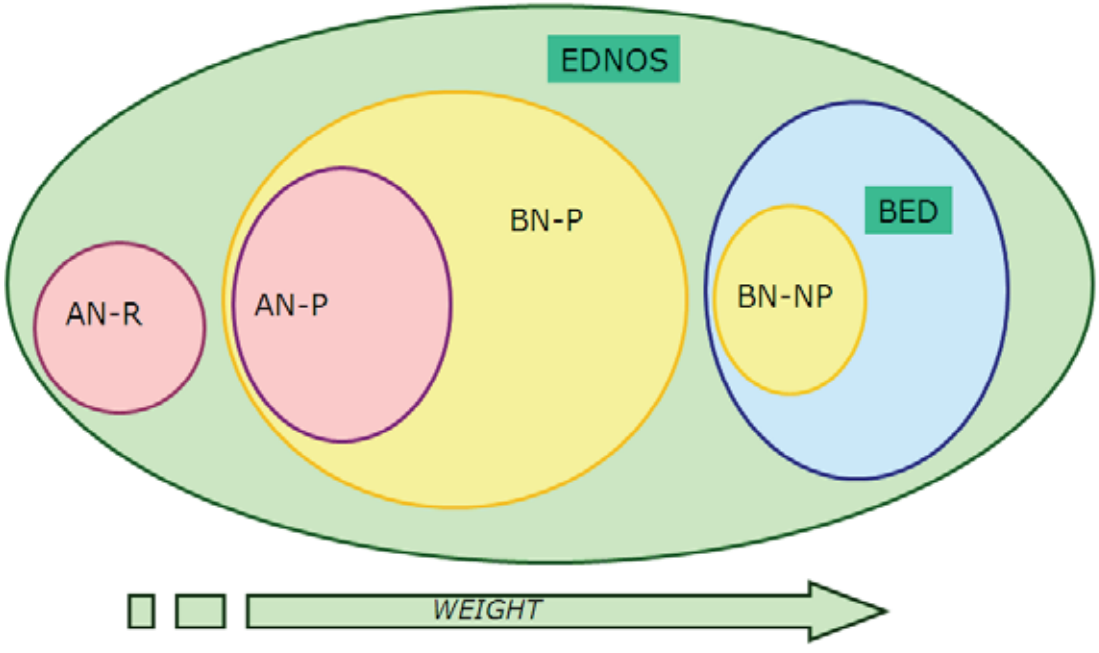
Study	Year	Source	Age	N	Screening	AN %	BN %
Button & Whitehouse	1981	College	16-22	446	EAT	0.2	---
Szmukler	1983	Private schools	14-19	1331	EAT	0.8	---
Szmukler	1983	State school	14-19	1676	EAT	0.2	---
Meadows, Palmer, Newball & Kenrick	1986	General practice	18-22	584	EAT	0.2	---
Johnson-Sabine, Wood, Patton, Mann & Wakeling	1988	Schoolgirls	14-16	1010	EAT	0	---
King	1989	General practice	16-35	539	EAT	0	---
Rastam, Gillberg & Garton	1989	Schoolgirls	15	2136	Growth chart and questionnaire	0.70	---
Bushnell. Wells, Hornblow, Oakley-Browne & Joyce	1990	Household census	18-24 25-44 (18-44)	777	DIS	---	4.5 2.0 (2.6)
Whitaker et al.	1990	High school	13-18	2544	EAT	0.3	4.2
Szabo & Tury	1991	Schoolgirls	14-18	416	EAT, BCDS, ANIS		0 0
Szabo & Tury	1991	College	19-36	224	EAT, BCDS, ANIS		4.0 1.3
Whitehouse, Cooper, Vize, Hill & Vogel	1992	General practice	16-35	540		0.2	1.5
Rathner & Messner	1993	Schoolgirls and case register	11-20	517	EAT	0.58	0
Santonastaso et al.	1996	Schoolgirls	16	359	EAT	---	0.5
Wlodarczyk-Bisaga & Dolan	1996	Schoolgirls	14-16	747	EAT	0	0
Steinhausen, Winkler & Meier	1997	Schoolgirls	14-17	276	EDE-S	0.7	0.5
Nobakht & Dezhkam	2000	Schoolgirls	15-18	3100	EAT	0.9	3.2
Gual et al.	2002	Schoolgirsl	12-21	2.862	EAT	0.3	0.8

Note: ANIS= Anorexia Nervosa Inventory Scale; EAT = Eating Attitudes Test: EDE-S= Eating Disorders Examination-Screening Version; BCDS= Bulimic Cognitive Distortions Scale

3. CLASSIFICATION AND DIAGNOSIS OF EATING DISORDERS

A prompt advancement in the categorization and comprehension of EDs has been achieved in a reasonably concise period of time. In the 1970s the first diagnostic criteria for AN were put forward. In 1979, BN was described for the first time and in the beginning of the 1980s, atypical EDs were identified. The fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (APA, 1994) is one of the most currently used classification manuals of EDs. It details three formal diagnoses of EDs; AN, BN, and EDNOS. Furthermore, the EDNOS category now entails a new specific ED subtype termed BED (*see figure 2*).

Figure 2: *Current Eating Disorder Diagnoses according to DSM-IV Criteria*



3.1 Anorexia Nervosa

The diagnostic criteria for AN of the DSM-IV (APA, 1994) are depicted in *table 2*. These criteria include preserving a body weight below 85% of usual weight for age and height, an extreme anxiety of gaining weight and dysfunctional attitudes about weight or shape that excessively affect self-evaluation. Furthermore, amenorrhea for a minimum of three successive menstrual periods is required (APA, 2000). The DSM-IV specifies two subtypes of AN; a "restricting type," typified by rigorous dieting or exercise without binge eating; and a "binge-eating/purging type," characterized by binge eating and/or purging behaviour by means of self-induced vomiting or abusing laxatives or diuretics. Even though the peak age range for the onset of AN has been revealed to be in adolescence, some individuals may also acquire AN in later adulthood (Abbate-Daga, Piero, Rigardetto, Gandione, Gramaglia, & Fassino, 2007; Hebebrand & Frey, 1999). The gender ratio for AN is approximately one man to ten women (APA, 2000).

Table 2: *DSM-IV Diagnostic Criteria for Anorexia Nervosa (APA, 1994)*

A. Refusal to maintain body weight at or above a minimally normal weight for age and height (e.g., weight loss leading to maintenance of body weight less than 85% of that expected; or a failure to make expected weight gain during period of growth, leading to body weight less than 85% of that expected).

B. Intense fear of gaining weight or becoming fat, even though underweight.

C. Disturbance in the way in which one´s body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or denial of the seriousness of the current low body weight.

D. In postmenarcheal females, amenorrhea, i.e., the absence of at least three consecutive menstrual cycles. (A woman is considered to have amenorrhea if her periods occur only following hormone, e.g., estrogen, administration).

Specify type:

Restricting Type: during the current episode of AN, the person has not regularly engaged in binge-eating or purging behaviour (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemassodes of binge eating).

Binge-Eating/Purging Type: during the current episode of AN, the person has regularly engaged in binge-eating or purging behaviour (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas).

3.2. Bulimia Nervosa

The DSM-IV (APA, 1994) criteria for BN are presented in *table 3*. BN is characterized by repeated occurrences of binge eating (defined by ingesting abnormally large quantities of food in a discrete period of time in addition to a subjective feeling of lack of control over eating). Furthermore, BN patients commonly utilize severe weight control methods (e.g., vomiting, laxative, diuretic or diet pill abuse, strict dieting or fasting and extreme exercising) and have negative body weight and shape experiences. In order to be able to diagnose a person with BN both the binge eating episodes and the inadequate weight control methods need to have occurred for a minimum of three months with a weekly frequency of at least twice per week. Two subtypes of BN are

detailed in the DSM-IV, a "purging type" and a "non-purging type", which is restricted to the rigorous weight control methods of dieting, fasting, or exercising without purging behaviour. Equally to AN, BN normally occurs in adolescence or early adulthood (Legenbauer & Herpertz, 2008).

Table 3: *DSM-IV Diagnostic Criteria for Bulimia Nervosa (APA, 1994)*

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:

(1) Eating, in a discrete period of time (e.g., within a 2-hour period), an amount of food that is definitely larger than most people would eat during a similar period of time and under similar circumstances.

(2) A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating).

B. Recurrent inappropriate compensatory behaviour in order to prevent weight gain, such as self-induced vomiting, misuse of laxatives, diuretics, enemas, or other medications, fasting, or excessive exercise.

C. The binge eating and inappropriate compensatory behaviours both occur, on average, at least twice a week for 3 months.

D. Self-evaluation is unduly influenced by body shape and weight.

E. The distribution does not occur exclusively during episodes of AN.

Specify type:

Purging type: during the current episode of BN, the person has regularly engaged in self-induced vomiting or the misuse of laxatives, diuretics, or enemas.

Non-purging type: during the current episode of BN, the person has used other inappropriate compensatory behaviours, such as fasting or excessive exercise, but has not regularly engaged in self-induced vomiting or the misuse of laxatives, diuretics, or enemas.

3.3. Eating Disorder Not Otherwise Specified

Although EDNOS has been found to be the most widespread subtype of EDs, there is a lack on the literature on this topic (Eddy, Celio Doyle, Hoste, Herzog, & le Grange, 2008a; Fairburn & Bohn, 2005; Turner, 2004). The DSM-IV criteria for EDNOS are outlined in *table 4*. Patients meeting criteria for EDNOS normally fail to encounter all the diagnostic conditions for one of the "official" EDs but they suffer similar important and clinically significant difficulties with eating and body image as AN and BN. Examples of behavioural profiles that would be suitable for such a diagnosis are outlined in the DSM-IV and are as follows: displaying all but one criterion for AN (e.g., low weight or amenorrhea), meeting all criteria for BN but not engaging in purging behaviour, or presenting all criteria for BN except for not meeting the frequency threshold (twice per week) for bingeing and purging (APA, 1994).

Table 4: *DSM-IV Diagnostic Criteria for Eating Disorder Not Otherwise Specified (APA, 1994)*

The Eating Disorder Not Otherwise Specified category is for disorders of eating that do not meet the criteria for any specific ED. Examples include:

1.) For females, all of the criteria for AN are met except that the individual has regular menses.

2.) All of the criteria for AN are met except that, despite significant weight loss, the individual´s current weight is in the normal range.

3.) All of the criteria for BN are met except that the binge eating and inappropriate compensatory mechanisms occur at a frequency of less than twice a week or for a duration of less than 3 months.

4.) The regular use of inappropriate compensatory behaviour by an individual of normal body weight after eating small amounts of food (e.g., self-induced vomiting after the consumption of two cookies).

5.) Repeatedly chewing and spitting out, but not swallowing, large amounts of food.

3.4. Binge Eating Disorder

Table 5 displays the DSM-IV (APA, 1994) criteria for BED, which is included as a temporary category of a precise example of EDNOS. It is described by persistent binge eating episodes with a frequency of at least two episodes per week over a six month period. Since binge eating episodes are not followed by compensatory weight control methods as it is the case in BN, individuals with BED generally experience intense feelings of guilt. In contrast to AN and BN, BED is not infrequent in males (about 1.5 female-to-male ratio) or ethnic minority groups. Furthermore, BED individuals are generally older than AN and BN at age of onset (between 30 and 50 years) (Fairburn, Cooper, Doll, Norman, & O'Conner, 2000; Striegel-Moore, 2007a; Striegel-Moore & Franko, 2003; Striegel-Moore, Wilfley, Pike, Dohm, & Fairburn, 2000; Wilfley, Friedman, Dounchis, Stein, Welch & Ball, 2000a). BED is also incorporated in Appendix B of the DSM-IV, which is set aside for potential new diagnostic categories that were not comprised in the DSM-IV due to the fact that there was not enough data to guarantee its inclusion (Bulik, Brownley, & Shapiro, 2007a; Bulik, Sullivan, & Kendler, 2003a).

Table 5: *DSM-IV Diagnostic Criteria for Binge Eating Disorder (APA, 1994)*

A.) Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:

(1) Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than most people would eat in a similar period of time under similar circumstances.

(2) A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating).

B. The binge-eating episodes are associated with three (or more) of the following:

(1) eating much more rapidly than normal

(2) eating until feeling uncomfortably full

(3) eating large amounts of food when not feeling physically hungry

(4) eating alone because of being embarrassed by how much one is eating

(5) feeling disgusted with oneself, depressed, or very guilty after overeating

C.) Marked distress regarding binge eating is present.

D.) The binge eating occurs, on average, at least 2 days a week for 6 months.

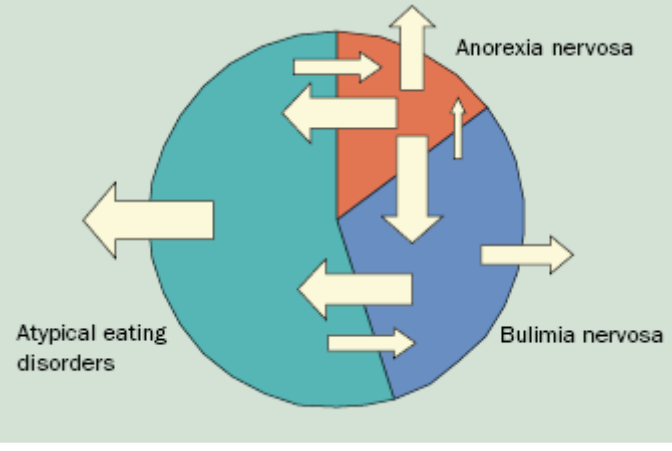
Note: The method of determining frequency differs from that used for BN. Future research should address whether the preferred method of setting a frequency threshold is counting the number of days on which binges occur or counting the number of episodes of binge eating.

E.) The binge eating is not associated with the regular use of inappropriate compensatory behaviours (e.g., purging, fasting, excessive exercise) and does not occur exclusively during the course of AN or BN.

3.5 Diagnostic crossover in eating disorders

Research on the diagnostic crossover in EDs has outlined that eating disturbed individuals have a propensity to wander between the different diagnostic categories of AN, BN and EDNOS *(see figure 3)*. Approximately 50% of AN patients go on to develop BN, around 30% of individuals with BN had previously presented a history of AN and yet another 30% had suffered from obesity in the past. This temporal movement indicates that all ED subtypes share common features. Conversely, evidence for the uniqueness of each diagnostic ED entity is provided by the fact that EDs do not develop into other illnesses (Anderluh, Tchanturia, Rabe-Hesketh, Collier, & Treasure, 2008; Eddy et al.,2008a; Fairburn & Harrison, 2003).

Figure 3: *Diagnostic crossover in Eating Disorders (Fairburn & Harrison, 2003)*



3.6 Categorical vs. Dimensional diagnosis of eating disorders

Some investigators have put into doubt the importance of some of the ED criteria outlined in the DSM-IV manual. Primarily, the weight threshold and the requirement for amenorrhea for AN has been put into question. Secondly, for BN, the frequency threshold for binge eating and purging episodes has been

debated. Finally, the association between the non-purging form of BN and BED still needs further illumination (Nunez-Navarro, Villarejo, Alvarez-Moya, Bueno, Jimenez-Murcia,& Granero et al., Submitted). Researchers have also indicated that certain diagnostic requirements for the official diagnoses of AN, BN and EDNOS are too rigid (Anderson, Bowers & Watson, 2001; Fairburn & Cooper, 2007a; Regier, 2007; Wonderlich, Crosby, Mitchell, & Engel, 2007a; Wonderlich, Joiner, Keel, Williamson, & Crosby, 2007b). All these issues therefore indicate that further research into the clinical characteristics of EDs is needed.

4. COMORBIDITY IN EATING DISORDERS

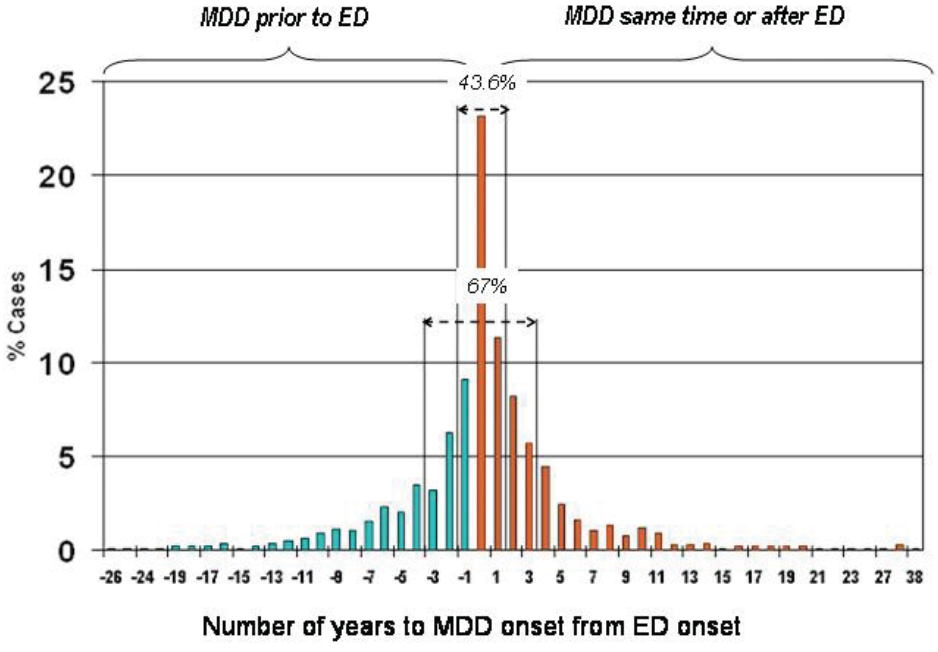
Research has indicated that 28% of individuals with any psychiatric illness have two or more comorbid lifetime diagnoses (Kessler, Berglund, Demler, Jin, Merikangas & Walters, 2005). Conversely, in ED patients this rate has been found to be as high as 50% in clinical and population-based psychiatric comorbidity studies (Bulik, Sullivan, & Kendler, 2000a; Fernandez-Aranda, Jimenez-Murcia, Alvarez-Moya, Granero, Vallejo, & Bulik, 2006; Pearlstein, 2002). Assessing the co-occurrence of psychiatric illnesses in EDs is important since it may increase the severity, chronicity and treatment resistance of these patients (Bulik, 2002).

4.1. Eating disorders and affective disorders

The association between EDs and affective disorders has been widely documented in the literature (Fernandez-Aranda, Pinheiro, Tozzi, Thornton, Fichter, Halmi et al., 2007; McElroy, Kotwal, Keck, & Akiskal, 2005; Pearlstein, 2002). Major depressive disorders (MDDs) and dysthymia are among the most commonly reported comorbid Axis I disorders in both individuals with AN and BN, with lifetime prevalence rates ranging from 20% to 83% (Iwasaki, Matsunaga, Kiriike, Tanaka, & Matsui, 2000; Perez, Joiner, & Lewinsohn, 2004; Spindler & Milos, 2004). Research has also steadily revealed that BED is related to augmented rates of lifetime MDD (46%-58%). Furthermore, the presence of axis I psychopathology has been found to distinguish obese women with BED from obese women without BED (de Zwaan, 2001; Wilfley, Schwartz, Spurrell, & Fairburn, 2000b). On the contrary, among patients with MDD, the prevalence of EDs does not differ significantly from the general population, with prevalence estimates varying from 4% to 10% (Zimmerman, Chelminski, & McDermut, 2002). As described in a recent study (Fernandez-Aranda et al., 2007a), in 1371 assessed ED patients, there were statistically significant differences in the prevalence of lifetime MDD across diagnostic subgroups. Individuals with ED subtypes that included either bingeing and/or purging behaviour reported greater lifetime MDD than individuals with the restricting subtype of AN (AN-R). Furthermore, in an analysis of the temporal pattern of the onset of MDD and EDs *(*see *figure 4)*, it was found that among all

individuals who had MDD before the ED, 26.5% had the MDD onset during the year previous to the onset of the ED and more than two-thirds (67%) of patients experienced the onset of both disorders within the same 3 year window.

Figure 4: *Relation of Age of Onset of Major Depressive Disorder (MDD) to Age of Onset of Eating Disorders*(Fernandez-Aranda et al., 2007a).*



*MDD=Major Depressive Disorder; ED= Eating Disorder; * Negative numbers indicate MDD came first.*

■ *MDD occurred prior to ED;* ■ *MDD occurred at the same time or after ED*

4.2. Eating disorders and anxiety disorders

The lifetime prevalence rates of anxiety disorders have been documented to be 20% to 55% in AN, 13% to 75% in BN and 9% to 46% in BED (Bulik, Sullivan, Carter, & Joyce, 1996; Godart, Flament, Lecrubier, & Jeammet, 2000; Iwasaki et al., 2000; Swinbourne & Touyz, 2007; Pearlstein, 2002). In comparison community based rates of 31% have been estimated (Kessler, McGonalge, Zhao, Nelson, Hughes, Eshleman et al., 1994). Social phobia, the most common anxiety disorder, has also been indicated to be significantly more frequent in EDs (prevalence rates of 55% for AN and 59% for BN) than in community women (prevalence estimate of 16%) (Kessler et al., 1994). Conversely, for BED, precise figures of the lifetime prevalence rates of social phobia are unavailable since rates have been found to vary tremendously (de Zwaan, 2001).

An elevated comorbidity between EDs and obsessive compulsive disorders (OCDs) has also been revealed. This co-occurrence together with phenomenological as well as clinical similarities have led numerous authors to suggest common etiopathogenic roots in the obsessive-compulsive spectrum for both disorders (Anderluh et al., 2008; Bienvenu, Samuels, Riddle, Hoehm-Saric, Liang, Cullen et al., 2000; Jimenez-Murcia, Fernandez-Aranda, Raich, Alonso, Krug, Jaurrieta et al., 2007). Evidences for a relationship between OCDs and EDs can be found in epidemiological data on comorbidity: the lifetime prevalence estimate of OCDs among individuals with EDs varies between 11% and 41%, whereas in OCD patients the prevalence rate of EDs ranges from 11% to 13% (de Mathis, do Rosario, Diniz, Torres, Shavitt, Ferrao et al., 2008; Halmi, Tozzi, Thornton, Crow, Fichter, Kaplan et al., 2005a; Micali & Heyman, 2006). A recent study (Bienvenu et al., 2000) reported that of 42 women with an OCD, 12% also presented with a lifetime prevalence for AN and 8% for BN.

4.3. Eating disorders and substance use disorders

Most studies have reported that EDs and substance use disorders (SUDs) frequently co-occur, with particularly high rates observed among patients in treatment (e.g., Gadalla & Piran, 2007; Holderness, Brooks-Gunn, & Warren, 1994; Pearlstein, 2002; Wolfe & Maisto, 2000). Lifetime prevalence rates of SUDs have been reported to be 12% to 18% in AN and 30% to 70% in BN, compared to 18% in community women (Blinder, Cumella, & Sanathara, 2006; Herpertz-Dahlmann, Muller, Herpertz, Heussen, Hebebrand, & Remschmidt, 2001). Rates of SUDs in the restrictive subtype of AN have been documented to be lower than rates in the binge/purging subtype of AN (Blinder et al., 2006; Iwasaki et al., 2000). Lifetime prevalence rates of SUDs in BED have been found to range from 8% to 33% (de Zwaan, 2001; Wilfley et al., 2000a,b).

4.4. Eating disorders and impulse control disorders

The few studies that have evaluated impulse control disorders (ICDs) in EDs, have reported a lifetime prevalence of between 10% and 19% (Grant & Kim, 2002; McElroy, 1999). The observed prevalence of lifetime ICDs among BN patients in a recent study was 23.8%, with compulsive buying and intermittent explosive disorder as the most frequently reported ICDs (Fernández-Aranda et al., 2006a). Accordingly, several studies have revealed higher prevalence rates of BN in a series of compulsive buyers compared to controls (Black, 1996; Black, Repertinger, Gaffney, & Gabel, 1998; Christenson, Faber, de Zwaan, Raymond, Specker, Ekem et al., 1994; Lejoyeux, Feuche, Loi, Solomon, & Ades, 1999). More recently, Mitchell and colleagues (2002) failed to demonstrate significant differences between healthy controls and compulsive buyers in the prevalence of current or lifetime EDs and eating-related psychopathology. Furthermore, the few studies where this topic was examined in more detail (Fernandez-Aranda et al., 2006; Fernandez-Aranda, Pinheiro, Thornton, Berrettini, Crow, Fichter et al., 2008) showed that the patients with BN and lifetime ICDs presented more extreme personality profiles, especially on novelty seeking and impulsivity, and greater general psychopathology than individuals with BN but without ICDs. This reflects research in other areas of psychiatry in which the presence of ICDs is commonly associated with greater

overall severity of the illness (Potenza, Fiellin, Heninger, Rounsaville, & Mazure, 2002).

4.5. Eating disorders and personality disorders

A few recent reviews (Cassin & von Ranson, 2005; Thompson-Brenner, Eddy, Franko, Dorer, Vashchenko, & Herzog, 2008a; Thompson-Brenner, Eddy, Satir, Boisseau, & Westen, 2008b; Lilenfeld, Wonderlich, Riso, Crosby, & Mitchell, 2006) on the comorbidity of personality disorders in EDs have revealed that compared to AN, BN patients suffered significantly more frequently from any Cluster B personality disorder (narcissistic, borderline, histrionic, and antisocial) (15% vs. 44%), with especially high rates observed in borderline personality disorder (14% vs. 31%). Cluster A (schizoid, schizotypal and paranoid) personality disorders were also higher in BN compared to AN (12% vs. 27%). Conversely, the frequency of Cluster C (dependent, avoidant, obsessive-compulsive and passive-aggressive) personality disorders was comparable for AN and BN with prevalence rates of about 45% for both disorders. Concerning BED, no specific personality disorders have been found to be elevated in these patients (Telch & Stice, 1998; Wilfley et al., 2000a,b).

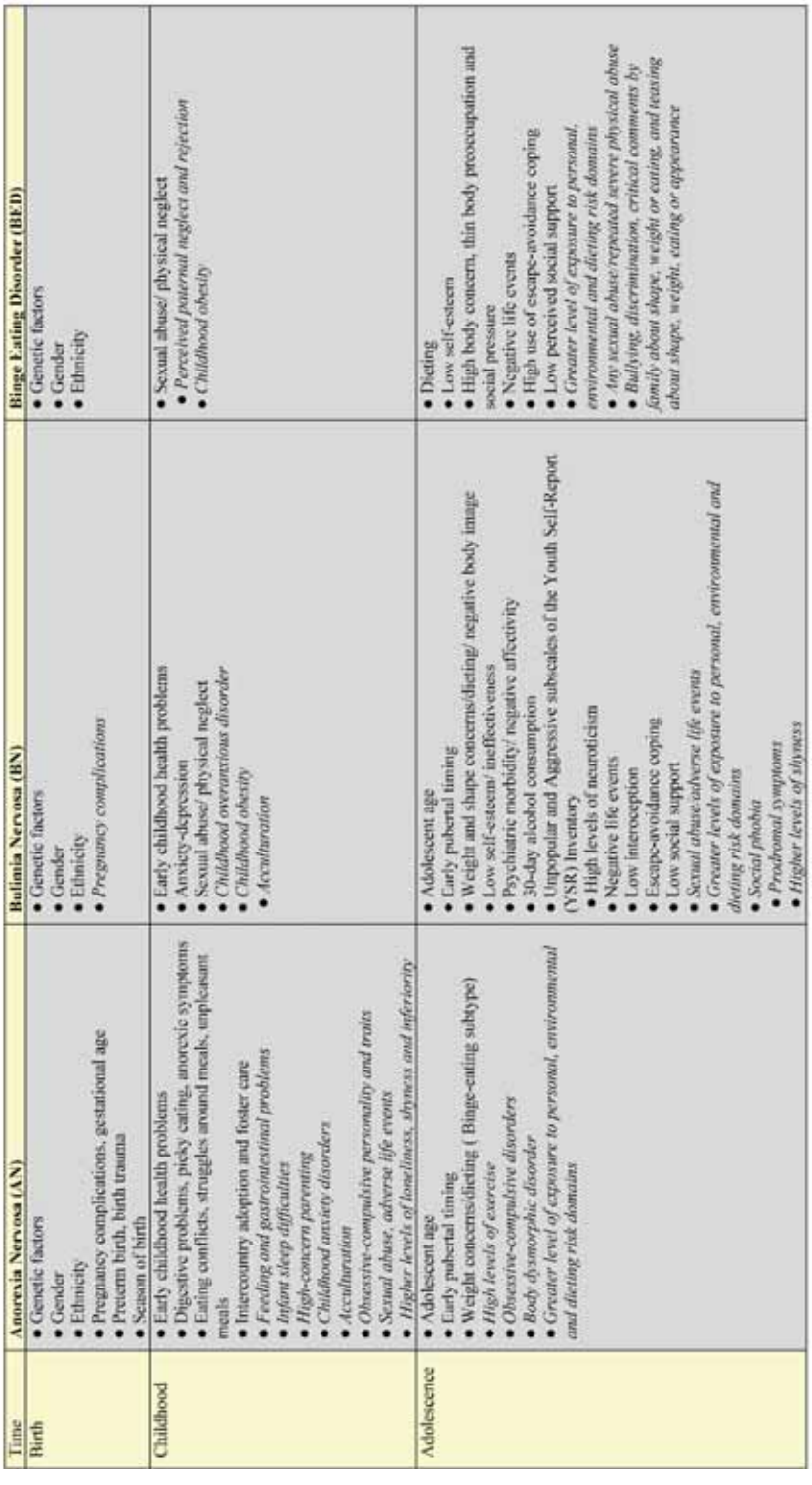
4.6. Problems associated with comorbidity studies of eating disorders

Research on the psychiatric comorbidity in EDs has suffered from various limitations, which need to be acknowledged and addressed in further research. Primarily, most studies have employed clinical samples, which may synthetically detect significant relationships that are not present in the community because of the discrepancy in referral (Cassin & von Ranson, 2005; Kessler et al., 2005; Pearlstein, 2002; Wu, Kouzis, & Leaf, 1999). Another limitation is that very few studies have utilized multivariable statistics to assess the correlations between EDs and comorbid disorders and therefore failed to control for additional psychopathology.

5. RISK FACTORS OF EATING DISORDERS: CORRELATES AND CONTRIBUTORY FACTORS

The aetiology of EDs remains poorly understood. Even though various psychological, social and biological factors have been implicated as potentially causal factors, few precise risk factors have been steadily replicated (Jacobi, et al., 2004). There are a number of recent reviews of risk factors for EDs in the literature from diverse viewpoints (e.g. Collier & Treasure, 2004; Mitchell & Bulik, 2006; Schmidt, 2003; Shisslak, Renger, Sharpe, Crago, McKnight, Gray et al.,1999; Stice, 2002; Striegel-Moore & Bulik, 2007b; Striegel-Moore, Dohm, Kraemer, Schreiber, Taylor & Daniels, 2007c). Nonetheless, only one review has attempted to elucidate the terminology of risk factors in EDs (Jacobi et al., 2004). In this review Jacobi and colleagues (2004) modelled on a time line several risk factors ranging from genes to ecological factors and focused their attention to their potency and specificity. Some of the most relevant risk factors in EDs have been summarized across AN, BN and BED subtypes and are displayed in *table 6*. Less is known about the contribution of risk factors for EDNOS since risk factor studies have generally tended to recruit true cases of AN and BN rather than broader, atypical cases. In comprehensive terms, the psychopathology of EDs is thought to develop from the interaction of numerous risk and protective factors which might be either biological or psychosocial in nature (Bulik, Heberbrand, Keski-Rahkonen, Klump, Reichborn-Kjennerud, Mazzeo et al., 2007; Schmidt, 2003; Stice, 2002).

Table 6: *Risk Factors and Retrospective Correlates* for AN, BN and BED (Jacobi et al., 2004)*



Time	Anorexia Nervosa (AN)	Bulimia Nervosa (BN)	Binge Eating Disorder (BED)
Birth	• Genetic factors • Gender • Ethnicity • Pregnancy complications, gestational age • Preterm birth, birth trauma • Season of birth	• Genetic factors • Gender • Ethnicity • *Pregnancy complications*	• Genetic factors • Gender • Ethnicity
Childhood	• Early childhood health problems • Digestive problems, picky eating, anorexic symptoms • Eating conflicts, struggles around meals, unpleasant meals • Intercountry adoption and foster care • *Feeding and gastrointestinal problems* • *Infant sleep difficulties* • *High-concern parenting* • *Childhood anxiety disorders* • *Acculturation* • *Obsessive-compulsive personality and traits* • *Sexual abuse, adverse life events* • *Higher levels of loneliness, shyness and inferiority*	• Early childhood health problems • Anxiety-depression • Sexual abuse/ physical neglect • *Childhood overanxious disorder* • *Childhood obesity* • *Acculturation*	• Sexual abuse/ physical neglect • *Perceived paternal neglect and rejection* • *Childhood obesity*
Adolescence	• Adolescent age • Early pubertal timing • Weight concerns/dieting (Binge-eating subtype) • *High levels of exercise* • *Obsessive-compulsive disorders* • *Body dysmorphic disorder* • *Greater level of exposure to personal, environmental and dieting risk domains*	• Adolescent age • Early pubertal timing • Weight and shape concerns/dieting/ negative body image • Low self-esteem/ ineffectiveness • Psychiatric morbidity/ negative affectivity • 30-day alcohol consumption • Unpopular and Aggressive subscales of the Youth Self-Report (YSR) Inventory • High levels of neuroticism • Negative life events • Low interoception • Escape-avoidance coping • Low social support • *Sexual abuse/adverse life events* • *Greater levels of exposure to personal, environmental and dieting risk domains* • *Social phobia* • *Prodromal symptoms* • *Higher levels of shyness*	• Dieting • Low self-esteem • High body concern, thin body preoccupation and social pressure • Negative life events • High use of escape-avoidance coping • Low perceived social support • *Greater level of exposure to personal, environmental and dieting risk domains* • *Any sexual abuse/repeated severe physical abuse* • *Bullying, discrimination, critical comments by family about shape, weight or eating, and teasing about shape, weight, eating or appearance*

5.1. Basic research: animal models and learning processes

The importance of animal models to human EDs have been outlined by some detailed reviews (Casper, Sullivan, & Tecott, 2008; Inoue, Iwasaki, Muramatsu, Yamauchi, & Kiriike, 2006; Treasure & Owen, 1997). Animal models of EDs are attractive because they allow the assessment of various manipulations under controlled conditions that would otherwise not be feasible. Furthermore, while in humans the disorder can only be examined after the illness has occurred, in animals researchers are able to assess cause-and-effect statements between precursors and succeeding behaviour.

5.1.1. Extreme Undereating

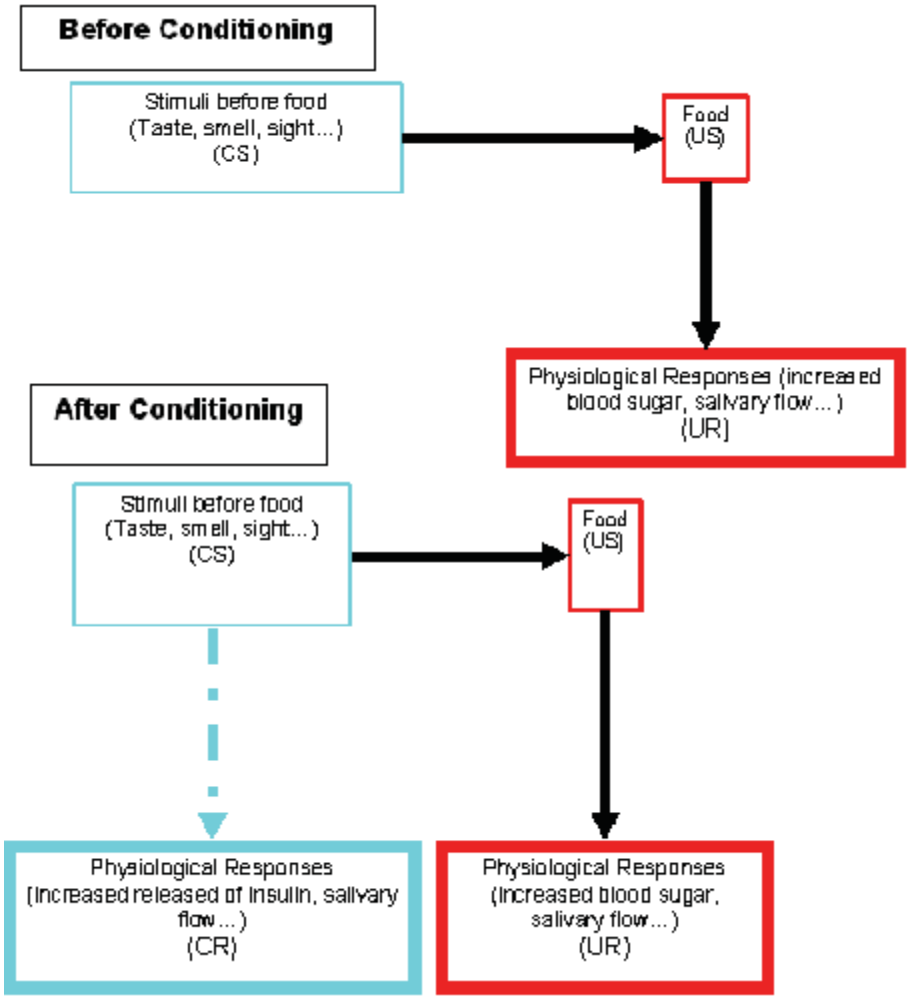
Generally research has documented that when animals are confronted with certain environmental stimuli which are believed to be important to human EDs (e.g. starvation, stress) they start displaying disordered eating behaviours. As regards to AN the most promising animal model to imitate AN is the activity-based AN (ABA) rodent model. This model states that after dietary restriction young female rats develop physical hyperactivity and self-starvation (Routtenberg & Kuznesof, 1967). New research findings have revealed that this phenotype can be saved by the peptide leptin, pointing out that this model is a well-situated pre-clinical tool for drug development in AN.

Other animal models of undereating also exist. Accordingly, social stress has been found to produce weight loss in subordinate animals (Tamashiro, Neguyen, Fujikawa, Xu, Yun Ma, Woods, et al., 2004; Tamashiro, Nguyen, & Sakai, 2005). Accordingly, Treasure and Owen (1997) reported that the lean sow syndrome develops in specific strains of pigs and is related to overactivity and other features of AN.

5.1.2. Extreme Overeating

The undereating of AN has often been documented to evolve into binge eating in rodents. As a result a variety of animal models of binge eating have been proposed (e.g. Boggiano, Artiga, Pritchett, Chandler-Laney, Smith, & Eldridge, 2007; Boggiano & Chandler, 2006; Corwin, 2006; Jansen, 1998) which generally entail a period of food restriction and an alternating accessibility of palatable food and stress. One of the models proposed to account for binge eating behaviour is Jansen´s (1998) theory of cue reactivity based on classical conditioning (illustrated in *figure 5*), which states that after systematic associations of cues (the conditioned stimulus, CS) with food (the unconditioned stimulus, US), the CS cues will reliably signal food. When these cues are good predictors of food, they acquire the ability to elicit adaptive physiological responses for digestion, such as salivation and insulin release. These classical conditioning responses (CRs) are supposed to be experienced as appetite, or even craving, and therefore increase the likelihood of food intake. This overeating might be linked to a disturbance in the chemistry of reward. A persistent priming of the reward circuits similar to the one found in addictions therefore takes place. Furthermore, not only do these animals overeat on palatable food but they are also more likely to acquire addictive behaviours when exposed to drugs (Avena & Hoebel, 2003; Thiele, Naveilhan, & Ernfors, 2004).

Figure 5 : *The Classical Conditioning Model of Binge Eating (Jansen, 1998)*



5.2. Heritability of eating disorder syndromes and symptoms

Familial aggregation in EDs has indicated an 11-fold elevated risk in first-degree family members of AN patients and a corresponding 4-fold relative risk for relatives of BN individuals (Klump, Kaye, & Strober, 2001; Kortegaard, Hoerder, Joergensen, Gillberg, & Kyvik, 2001; Lilenfeld, Kaye, Greeno, Kerikangas, Plotnicov, Pollice et al., 1998; Strober, Freeman, Lampert, Diamond, & Kaye, 2000). Heritability rates for EDs have been found to vary from 48% to 88% for AN, 28% to 83% for BN and 40% to 82% for BED (Bulik,

Wade, & Kendler, 2001; Bulik, Sullivan, Tozzi, Furberg, Lichtenstein & Pederson, 2006; Mercader, Ribases, Gratacos, Gonzalez, Bayes, de Cid, et al., 2007a; Ribases, Gratacos, Fernandez-Aranda, Bellodi, Boni, Anderluh et al., 2005).

Behavioural traits and psychopathological symptoms such as the Eating Disorder Inventory (EDI-II) (Garner, 1991) subscales 'drive for thinness' and 'body dissatisfaction' have been indicated to have a genetic risk of 44% and 52%, respectively. As regards to self-induced vomiting, a heritability rate ranging from 60% to 83% has been documented. Disinhibition of eating and restrained eating on the other hand have revealed a genetic transmission of 40% and 48% respectively (Steinle, Hsueh, Snitker, Pollin, Sakul, St Jean, et al., 2002). Finally the heritability of purely binge eating behaviour without compensatory behaviours has been estimated to be 41% (Wade, Bulik, Neale, & Kendler, 2000). Binge eating behaviour has also been assessed as a possible transitional behavioural phenotype in the understanding of the genetics of obesity and has been pinpointed as a vital phenotypic characteristic of individuals with a mutation in the melanocortin 4 receptor (MC4R), a candidate gene thought to affect eating behaviour (Branson, Potoczna, Kral, Lentes, Hoehe & Horber, 2003). However, this finding still requires further replication (Hebebrand, Geller, Dempfle, Heinzel-Gutenbrunner, Raab, Gerber, et al., 2004).

5.3. Molecular genetics and neurobiology

Biological studies of EDs have proposed an important disruption in the serotonergic function in BN patients (Frank, Bailer, Henry, Wagner, & Kaye, 2004; Steiger, Gauvin, Israel, Kin, Young & Roussin, 2004). Concerning AN, candidate gene association analysis has identified a susceptible risk allele in the brain derived neurotrophic factor (BDNF) gene (Ribases, Gratacos, Armengol, de Cid, Badia, Jimenez et al., 2003; Ribases et al., 2005) and the serotonin receptor gene 5HT2A (Collier, Arranz, Li, Mupita, Brown, & Treasure, 1997). Other neurotransmitter systems, especially dopamine, have also been found to be implicated in EDs (Barbarich, Kaye, & Jimerson, 2003). Ultimately our

group has characterized the role of a neurotrophin signalling pathway in the development of EDs (Mercader, Saus, Aguera, Bayes, Boni, Carreras et al., 2008; Mercader, Fernandez-Aranda, Gratacos, Ribases, Badia, Villarejo, et al., 2007b; Ribases, Gratacos, Fernandez-Aranda, Bellodi, Boni, Anderluh et al., 2004). However, the effect size of these variants does not account for the 50% heritability estimates, which indicates that many vulnerability genes still need to be discovered.

5.4. Familial psychopathology

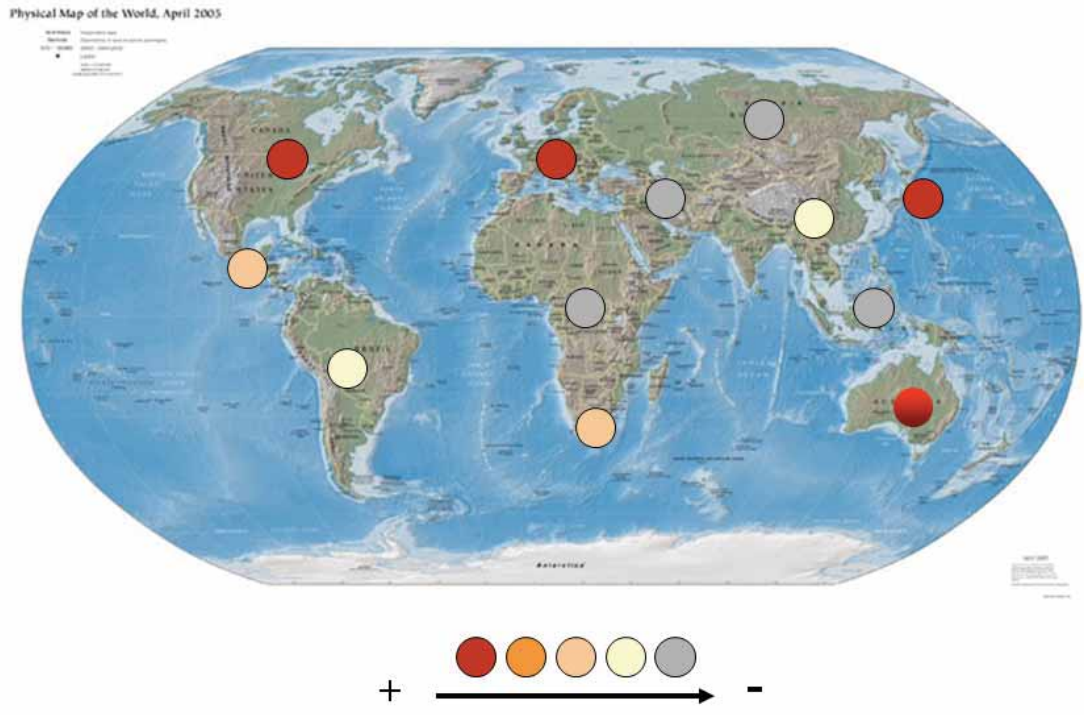
Given the high levels of comorbidity between EDs and other psychiatric disorders the question arises to what extent a co-aggregation among family members exists (Schmidt, 2003). As regards to mood disorders, family studies have indicated an elevated morbidity risk for EDs and mood disorders, in spite of the fact that the estimates of magnitude of this co-aggregation have been reported to vary from slight to strong (Hudson et al., 2001; Mangweth, Hudson, Pope, Hausmann, De Col, Laird et al., 2003). A shared susceptibility risk for obsessive-compulsive spectrum disorders in first-degree relatives of ED probands has also recently been documented in the literature (Bellodi, Cavallini, Bertelli, Chiapparino, Riboldi, & Smeraldi, 2001). Finally, research on the familial relationships between personality traits and EDs has been contradictory with some studies suggesting familial co-transmission (Kendler, Walters, Neale, Kessler, Heath, & Eaves, et al., 1995; Lilenfeld, Stein, Bulik, Strober, Plotnicov, Pollice et al., 2000) and others disputing this (Carney & Cizaldo, 1990).

5.5. Sociocultural risk factors

Eating disorders are typically characterized as Western culture-bound syndromes associated with culture-driven factors such as an extreme adoption of the slim social ideal, transitions in the role of women, and undesirable social standards and attitudes towards overweight (Keel & Klump, 2003). All forms of socio-cultural pressures (e.g. media, peer-group pressure, and participation in certain at-risk groups or activities such as gymnastics) have therefore been blamed to promote body image dissatisfaction and disordered eating pathology

(Haines & Neumark-Sztainer, 2006a; Haines, Neumark-Sztainer, Eisenberg, & Hannan, 2006b; Keery, van den Berg, & Thompson, 2004; McLaren & Kuh, 2004a,b). Nonetheless, the fact that only the minority of women residing in Western countries go on to develop EDs indicates that these socio-cultural influences are neither indispensable nor enough to account for the development of EDs. The distribution of EDs across the world is illustrated in *figure 6*.

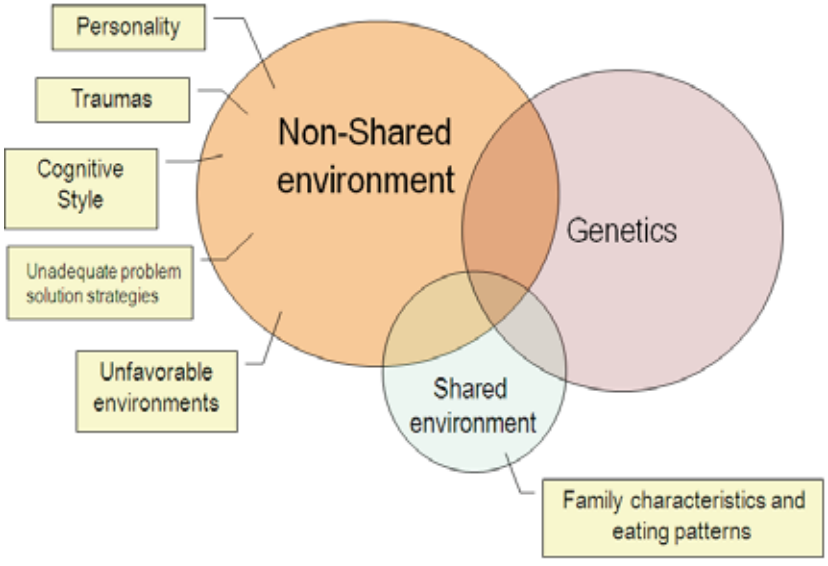
Figure 6: *Distribution of Eating Disorders across the World*



Research has indicated that EDs are made up of both genetic and environmental risk factors. Environmental factors can be either shared (e.g. parental divorce) or non-shared (e.g. individual experience of abuse) (*see figure 7*). More recently investigators have started to pay specific attention to the non-shared environmental factors, which function within families to make members unique rather than similar to each other. The findings obtained from these studies (e.g. Bulik, Sullivan, Wade, & Kendler, 2000) have indicated that ED patients are made up virtually completely of genetic and non-shared environmental factors

(Bulik, Sullivan, Wade, & Kendler, 2000b; Plomin, Asbury, & Dunn, 2001a; Plomin & Craig, 2001b). When assessing the risk factors implicated in the development of EDs, it is therefore essential to concentrate on the precise individual non-shared environmental factors.

Figure 7: *Genetic and Shared versus Non-shared Environmental Factors of Eating Disorders*



5.6.1. Individual and family risk factors of eating disorders

The literature has shown that the family context plays an important role in the development and maintenance of EDs (Bean & Weltzin, 2001; Micali, Holliday, Karwautz, Haidvogel, Wagner, & Fernandez-Aranda, et al., 2007; Senra, Sanchez-Cao, Seoane, & Leung, 2007). Family dynamics characterized by abuse and neglect or cold, unsupportive relationships are a robust predictor of a wide range of child physical and mental health outcomes including eating psychopathology (Jones, Harris, & Leung, 2006; Okon, Greene, & Smith, 2003). However, only a few studies have valued the psychometric properties of specific ED assessment instruments that include the individuals' early environment and

family behaviours. Therefore, familiar risk factors are often captured using unavailable tools.

5.6.2. Personality traits in eating disorders

Numerous studies have shown that personality traits are shared by patients with EDs (Alvarez-Moya, Jimenez-Murcia, Granero, Vallejo, Krug. & Bulik et al., 2007; Thompson-Brenner et al., 2008a,b; Vervaet, van Heeringen, & Audenaert, 2004). Most of these studies have found that restrictive AN individuals are commonly characterized as being perfectionist, persistent, anxious, harm-avoidant, obsessive, compulsive and low on novelty seeking and self-directedness. The personality features of BN are more heterogeneous with impulsivity and emotional instability being the most prevalent traits. However perfectionism, harm avoidance, compulsivity and obssesionality have also often been documented in these patients (Klump, Bulik, Pollice, Halmi, Fichter, & Berrettini, et al., 2000). Research has indicated that several of these personality traits remain even after recovery (Wagner, Barbarich-Marsteller, Frank, Bailer, Wonderlich, & Crosby et a., 2006). While some researchers have proposed that such findings are suggestive of a premorbid personality susceptibility, others have questioned this standpoint by arguing that these features might also be indicative of a scaring effect of the eating pathology (von Ranson, Kaye, Weltzin, Rao, & Matsunaga, 1999; Wagner et al., 2006).

5.6.3. Cognition and negative affect in eating disorders

Disturbances in several cognitive areas (e.g., impaired schema structures of weight and one's own body, low self-esteem and high perfectionism) have been reported to be predisposing factors for EDs and have been found to encourage an extreme need to control eating, place a high value on attaining an idealized weight and body shape and reinforce the maintenance of the problem through nutritional-dietary restrictions (Eiber, Mirabel-Sarron, & Urdapilleta, 2005; Kyriacou, Treasure, & Schmidt, 2008; Lena, Fiocco, & Leyenaar, 2004).

Although a temperamental characteristic such as negative emotionality is improbable to lead to EDs in and of itself, negative affect has commonly been implicated in the development of EDs (e.g., Truglia, Mannucci, Lassi, Rotella, Fravelli, & Ricca, 2006; Wilfley et al., 2000a). ED patients, in particular BN individuals, have for example been found to exhibit elevated self-directed hostility scores and suppressed anger (Fassino, Daga, Piero, Leombruni, & Rovera, 2001; Geller, Cockell, & Goldner, 2000). More specifically, negative affect has been revealed to mediate the relation between dieting and binge eating, even though dieting and negative affect remain independent predisposing factors for binge eating (Arnow, Kenardy, & Agras, 1995; Engelberg, Steiger, Gauvin, & Wonderlich, 2007). It may, therefore be that negative affectivity increases susceptibility for overall psychopathology rather than EDs per se (Truglia et al., 2006).

5.6.4. Neuropsychological vulnerabilities in eating disorders

As regards to the neuropsychological vulnerabilities in EDs, the majority of studies until now have focused on AN patients (Black, Wilson, Labouvie, & Heffernan, 1997; Dobson & Dozois, 2004; Duchesne, Mattos, Fontenelle, Veiga, Rizo, & Appolinario, 2004; Rofey, Corcoran, & Tran, 2004). In general, these studies found set-shifting difficulties (poor cognitive flexibility), poor central coherence (tendency to focus on details instead of the whole), and attentional impairments (Duchesne et al., 2004; Lopez, Tchanturia, Stahl, & Treasure, 2008; Roberts, Tchanturia, Stahl, Southgate, & Treasure, 2007; Rofey et al., 2004; Tchanturia, Campbell, Morris, & Treasure, 2005). However, some studies suggest that these deficits are state dependent, and therefore disappear after recovering from AN (Gillberg, Rastam, Wentz, & Gillberg, 2007). Comparative studies of BN patients have indicated that the neurocognitive performance of these patients is similar to the one of restrictive AN patients. (e.g., Cooper, Wood, Orcutt, & Albino, 2003; Perpina, Hemsley, Treasure, & de Silva, 1993). In BN patients impairment of selective attention, abilities of problem solving, executive functioning, set-shifting, central coherence, speed of information processing and cognitive inhibition have been documented (Black et al., 1997; Dobson & Dozois, 2004; Lauer, Gorzewski, Gerlinghoff, Backmund, & Zihl, 1999; Lopez et al., 2008; Roberts et al., 2007).

6. TREATMENT OF EATING DISORDERS

Professional organizations have developed several English-language treatment guidelines for the treatment of EDs. These include the American Psychiatric Association (APA, http://www.psych.org/), American Academy of Pediatrics (AAP, http://www.aap.org/), the Society for Adolescent Medicine (SAM, http://www.adolescenthealth.org/), the Royal Australian and New Zealand College of Psychiatrists (RANZCP, http://www.ranzcp.org/) and the National Institute for Clinical Excellence (NICE) http://www.nice.org.uk/).

The NICE recommendations (Wilson & Shafran, 2005) are allocated a grade ranging from A (solid empirical evidence from well-performed randomized trials) to C (expert judgment without robust empirical support). *Figure 8* shows the psychosocial and biological treatments generally employed for EDs. Fairburn and Harrison (2003) have outlined a table with the empirical standing of treatments advocated for patients with EDs, which can be found in *table 7.*

Figure 8: *Psychosocial and Biological Treatments for Eating Disorders*

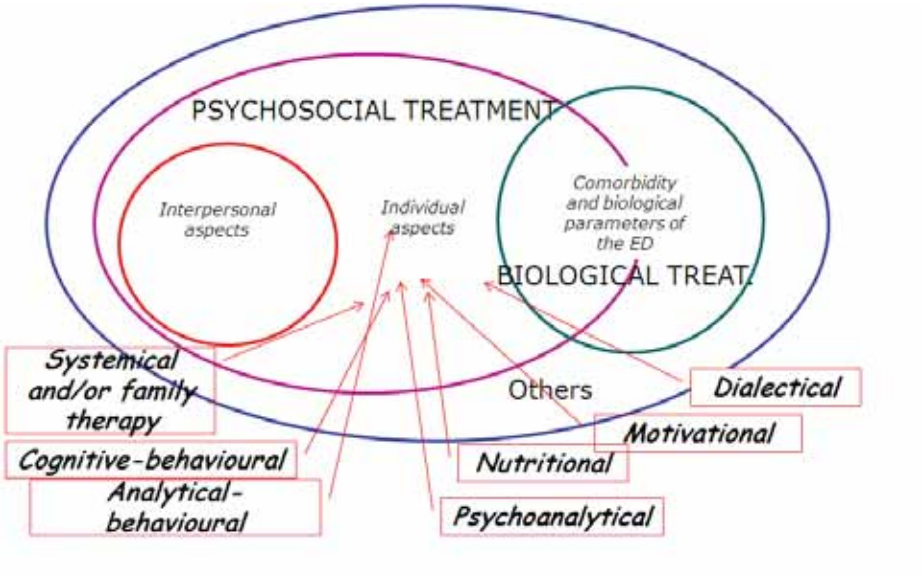


Table 7: *Empirical Standpoint of Treatments advocated for Patients with Eating Disorders (Fairburn & Harris, 2003).*

Treatment	Anorexia Nervosa		Bulimia Nervosa		Atypical eating disorders		Binge eating disorder	
Drug treatment	Evidence	Effect	Evidence	Effect	Evidence	Effect	Evidence	Effect
Antidepressants (acute treatment)	Modest	0	Considerable	**	None	-	Modest	**
Antidepressants (relapse prevention)	Modest	*	Modest	*	None	-	None	-
Antipsychotics	Modest	0	None	-	None	-	None	-
Appetite suppressants	None	-	Modest	0	None	-	Modest	**
Psychological Treatment								
Cognitive analytic therapy (CAT)	Modest	*	None	-	None	-	None	-
Cognitive behaviour therapy (CBT)	Modest	*	Strong	***	None	-	Moderate	***
"Dialectical behaviour therapy"- based treatment	None	-	Modest	**	None	-	Modest	**
Exposure with response prevention (ERP)	None	-	Moderate	**	None	-	None	–
Family-based therapy for adolescents	Moderate	***	None	-	None	-	None	-
Interpersonal psychotherapy (IPT)	None	-	Moderate	**	None	-	Modest	***
Nutritional counselling	Modest	0	Modest	*	None	-	None	-
Psychodynamic psychotherapy	Modest	*	Modest	*	None	-	None	-
Psychoeducational self-help	None	-	Moderate	*	None	-	Moderate	**
Schema-based cognitive therapy	None	-	None	-	None	-	None	-
12-step approaches	None	-	None	-	None	-	None	-

Weight of evidence: none= no studies done, modest= fewer than four trials (none of superior quality), moderate= at least four trials or two trials of superior quality, considerable=rating between moderate and strong, strong= at least ten trials and at least five trials of superior quality. Magnitude of effect: - = treatment not studied, 0= no beneficial effect, *= slight beneficial effect, **= some beneficial effect, ***= moderate beneficial effect, ****= pronounced beneficial effect- i.e., substantial and persistent effect.

6.1. Anorexia nervosa

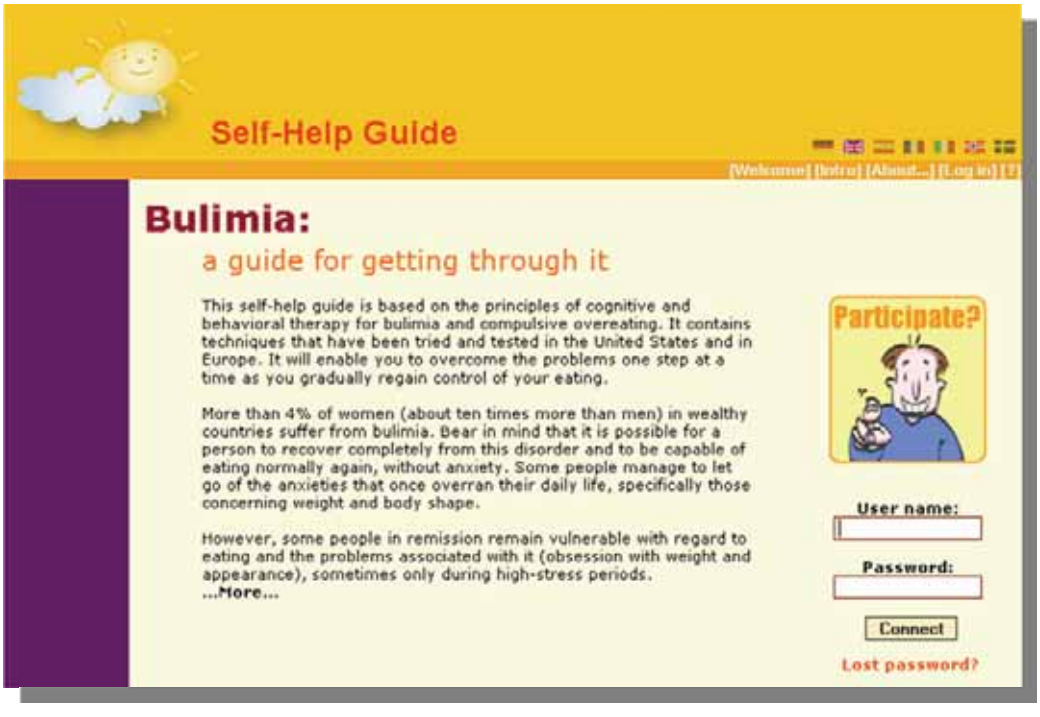
The first line treatment for AN is typically centred on instant weight gain, particularly with those who are in a remarkably critical state that may demand hospitalization. However, most AN patients are treated as outpatients, ideally with the contribution from a mixture of different health professionals (Bulik, Berkman, Brownley, Sedway, & Lohr, 2007; Schmidt et al., 2007). The evidence for treatment of AN is tremendously restricted. In the recent NICE guidelines only one study (family therapy for adolescents) achieved the "B" quality criteria (Wilson & Shafran, 2005) and there was no study with a grade "A". As regards to drugs, there is no support that any pharmaceuticals have an effect on weight increase for AN. Apart from the NICE guidelines there are a number of other systematic reviews which have also concluded that the evidence for the effectiveness of AN treatment until the present moment is inadequate (Bulik et al., 2007c; Treasure & Schmidt, 2002). One study (Halmi, Tozzi, Thornton, Crow, Fichter, & Kaplan, et al., 2005b), published after the last update of the NICE guidelines in 2004, has even questioned whether it was feasible to use randomised trials for AN as the adequacy of some treatments was so minimal.

6.2. Bulimia nervosa

The clinical appearance and the context of treatment in BN patients is more consistent than for AN, and therefore BN patients are generally treated in out-patient settings (Fernández-Aranda, Casasnovas, Jimenez-Murcia, Krug, Martinez, & Nunez et al., 2004; Schmidt, Lee, Beecham, Perkins, Treasure, & Yi et al., 2007; Shapiro, Berkman, Brownley, Sedway, Lohr & Bulik, 2007). Several controlled studies have shown that cognitive behavioural therapy (CBT) and interpersonal therapy (IPT) are the two most effective approaches in the treatment of BN (Fairburn, Jones, Peveler, Hope, O'Conner, 1993a; Fairburn, Marcus, & Wilson, 1993b), with CBT leading to more rapid symptomatic change (Fairburn, 1997). The NICE guidelines have therefore outlined a grade "A" for CBT and a grade "B" for antidepressant interventions for BN (Wilson & Shafran, 2005). Research into the treatment of BN has also been summarized in several recent reviews (Bacaltchuk & Hay, 2003; Bacaltchuk, Trefiglio, de Oliveira, Lima, & Mari, 1999; Shapiro et al., 2007). Guided treatment delivering

CBT through books (Schmidt & Treasure 1993), computer-or a web-based programme (Bara-Carril, Williams, Pombo-Carril, Reid, Murray, & Aubin et al., 2004; Carrard, Rouget, Fernandez-Aranda,Volkart, Damoiseau, & Lam, 2006) have also been fruitfully employed in the management of BN. Furthermore, as with other psychiatric disorders (Mimeault & Morin, 1999), several studies on BN have shown that alternative brief interventions or non-therapist-led approaches seem to be effective, especially in those patients with less severe symptoms (Fernandez-Aranda, Sanchez, Turon, Jimenez, Alonso, & Vallejo, 1998a; Olmsted, Davis, Garner, Eagle, Rockert, & Irvine, 1991).

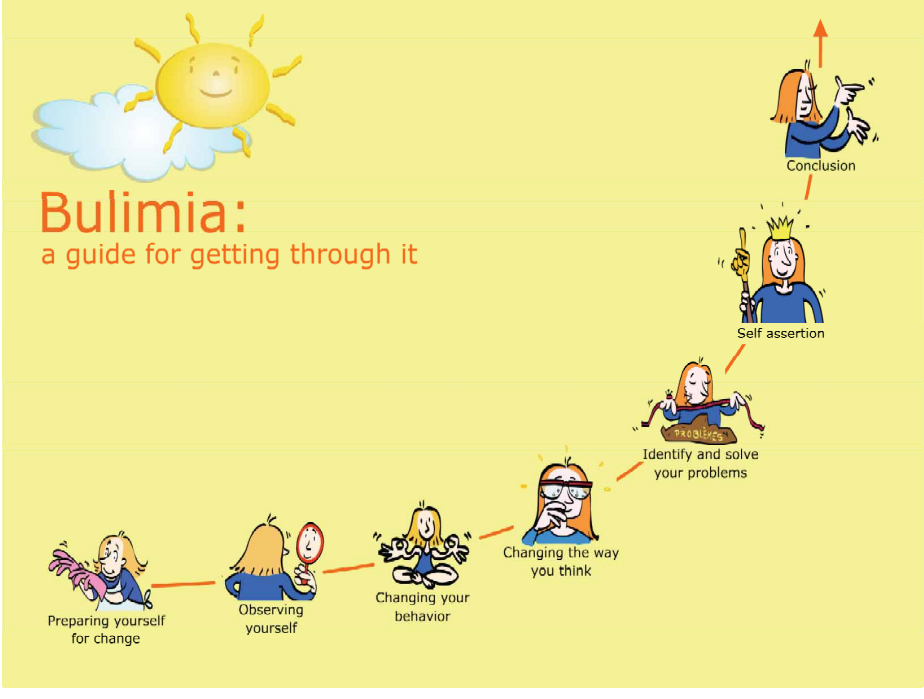
Figure 9: *An Internet-Based Self Help Guide for Bulimia Nervosa: Welcoming Page*



6.3. Binge eating disorder

Most of the treatments applied in BN have been implemented for the management of BED (Brownley, Berkman, Sedway, Lohr, & Bulik, 2007). According to the NICE guidelines, CBT was advocated an ”A” grade. More recently, antidepressant [selective serotonin reuptake inhibitors (SSRIs)], anti-obesity and anti epileptic/mood stabilizer drugs have been found to be effectual in weight decrease (Arnold, McElroy, Hudson, Wedge, Bennett & Keck, 2002). As regards to obese patients with binge eating, sibutramine, a specific reuptake noradrenaline and serotonin inhibitor (SNRI) has been used and found to diminish both weight and binge eating occurrences (Appolinario, Bacaltchuk, Sichieri, Claudino, Godoy-Matos, & Morgan et al., 2003). A recent systematic review of randomized controlled trials in BED has been published by Brownley and colleagues (Brownley et al., 2007).

Figure 10: *An Internet-Based Self Help Guide for Bulimia Nervosa: The 7 Steps of Treatment*



6.4. Atypical eating disorders

There has been no research on the treatment of atypical EDs other than the promising effort on BED. For this reason the NICE guidelines highlight the lack of adequate support for the management of atypical EDs, for which guidelines are reduced to recommending that "the clinician considers following the guidance on the treatment of the eating problem that most closely resembles the individual patient´s ED" (Wilson & Shafran, 2005).

6.5. Outcomes of Eating Disorders

A review by Steinhausen (2002) has uncovered that AN patients have a 50% possibility of recuperation within 10 years after the beginning of the illness, 25% develop into chronicity, and mortality rates have been shown to be as high as 25%. A comparable outcome has been reported by (Pike, 1998) in a wide-ranging review of more than 150 studies investigating the long-term outcome of AN. Conversely, some less optimistic findings were uncovered in a study by Fichter and Quadflieg (1999), in which less than 25% of the patients were in full remission at follow-up after 6 years.

In general, individuals with BN have been located to encompass a better prognosis than AN. Short term studies found that about 50% of people made a full recovery, 30% made a partial recovery, and 20% continued to have symptoms (e.g., Keel & Mitchell, 1997). Similar results were found from longitudinal studies. A 10 year follow up study for instance revealed that 52% had recovered fully and only 9% continued to experience bulimic symptoms (Collings & King, 1994). Another study found that after a mean follow up of 11.5 years, 11% still met criteria for BN, whereas 70% were in full or partial remission (Keel, Mitchell, Miller, Davis, & Crow, 2000).

To date, various investigations have tried to determine which factors are related with either a good or poor outcome of EDs (e.g., (Berkman et al., 2007; Steinhausen, 2002; Steinhausen, Grigoroiu-Serbanescu, Boyadjieva, Neumarker, & Winkler Metzke, 2008). Baseline predictors of outcome include bingeing and vomiting frequency, duration of the disorder (Turnbull et al., 1997), history of body weight (Agras, Crow, Halmi, Mitchell, Wilson, & Kraemer, 2000a; Agras, Walsh, Fairburn, Wilson, & Kraemer, 2000b; Fairburn, Agras, Walsh, Wilson, & Stice, 2004), level of general psychiatric symptoms (Agras et al., 2000a; Bulik, Sullivan, Joyce, Carter, & McIntosh, 1998; Fairburn et al., 2004), history of substance abuse (Wilson, 1999) and personality traits such as self-directedness (Bulik, Sullivan, Carter, McIntosh, & Joyce, 1999).

The clinical prognosis of ED patients appears however to be difficult to forecast since the course of the disorders is tremendously changeable and the long-term outcomes of treatments are uncertain. In addition, since eating-disordered patients might have low motivation to seek and adhere to treatment, they often drop out of treatments. Also relapse rates following discharge are generally high and can take place even years after an episode of comparatively decent health (Kordy, Kramer, Palmer, Papezova, Pellet, & Richard et al., 2002).

To summarize, notwithstanding the observation that at least half the causes of EDs are non-genetic in origin, social, cultural and individual specific environmental factors have scarcely been assessed. The role of most risk factors outlined in the literature on the development of EDs is therefore unclear and is further hampered by small sample sizes and shortcomings in the methodology employed. The literature on the treatment efficacy and outcome for EDs is also highly inconsistent in quality, with the principal imperfection resting on the treatment of AN. Finally, the neglect of the atypical EDs is also a source of concern.

7. APPROACH AND GENERAL OBJECTIVES

The main objective of the present thesis is to refocus ED research into the neglected areas of psychological and environmental factors. Therefore the full potential of psychological and environmental information to combat EDs will be used by employing an interactive and translational approach running from basic science through to the clinic. In order to make the data obtained from the present studies more comprehensible, the present thesis will be subdivided into three major areas which are: a.) clinical factors and comorbidity (namely substance use in EDs); b.) psychological, behavioural and environmental correlates of EDs and c.) treatment effectiveness in EDs.

7.1. Main Objectives

7.1.1. Primary objectives:

1.) To evaluate the co-occurrence of substance use in women with EDs.

2.) To assess the susceptibility to overeating in animals through classical contextual conditioning.

3.) To identify the psychological and environmental factors (e.g. early individual and family eating patterns and anger expressions) associated with the development and maintenance of EDs.

4.) To assess the efficacy of outpatient therapeutical interventions in EDs.

7.1.2. Secondary objectives:

1.) To examine differences across diagnostic categories (AN, BN and EDNOS) in substance use, early individual and family eating behaviours, anger expressions and treatment effectiveness.

2.) To assess cultural variation in substance use and early individual and family eating behaviours, by assessing the data from five different European countries (Spain, Austria, UK, Slovenia and Italy).

3.) To explore the relation among ED symptoms, comorbid symptomatology, personality traits, and impulsive behaviours.

7.2. Main hypothesis

1.) Substance use will be higher in individuals with EDs than in matched controls.

2.) Contextual cues related to food intake will elicit higher food consumption in rats than alternative contexts which had never been paired with food intake.

3.) Certain individual and family eating patterns and food choices during childhood and early adolescence will be related to the development of a subsequent ED.

4.) Maladaptive anger expressions will be higher in ED patients than in healthy controls.

5.) There will be cross-cultural differences in ED correlates as regards to substance use and early individual and family eating patterns across various European countries.

6.) Differences across ED subtypes exist in substance use, early eating behaviours, anger expressions and treatment effectiveness.

7.3. The articles included in the thesis

A.) Clinical factors and comorbidity in eating disorders

Study 1: Calero, A., **Krug, I.,** Davis, K., Lopez, C., Fernández-Aranda, F., & Treasure, J. (Submitted). Meta-Analysis on drugs in people with eating disorders.

Study 2: Krug, I., Poyastro Pinheiro, A., Bulik, C., Jiménez-Murcia, S., Granero, R., Penelo, E., Masuet, C., Aguera, Z., & Fernández- Aranda, F. (In press). Lifetime substance abuse, family history of alcohol dependence and novelty seeking in eating disorders: A comparison study of eating disorders subgroups. Psychiatry and Clinical Neurosciences.

Study 3: Krug I., Treasure, J., Anderluh, M., Bellodi, L., Cellini, E., di Bernardo, M., Karwautz, A., Nacmias, B., Ricca, V., Sorbi, S., Tchanturia, K., Wagner, G., Collier, D., & Ferandez-Aranda, F. (2008). Present and lifetime comorbidity of tobacco, alcohol and drug use in eating disorders: A European Multicenter study. Drug and Alcohol Dependence, 97, 169-179.

B.) Psychological, behavioural and environmental correlates of eating disorders

Study 4: Sansa, J., **Krug, I.,** Chamizo, V.D., & Fernandez-Aranda, F. (In press). An animal model of learning in binge eating: the role of cotnextual conditioning and food density. Psicologica: International Journal of Methodology and Experimental Psychology

Study 5: Fernández-Aranda, F., **Krug, I.,** Granero, R., Ramón, JM., Badia, A., Giménez, L., Solano, R., Collier, D., Karwautz, A., & Treasure, J. (2007). Individual and family eating patterns during childhood and early adolescence: an analysis of associated eating disorder factors. Appetite, 49, 476–485.

Study 6: Krug, I., Treasure, J., Anderluh, M., Bellodi, L., Cellini, E., Collier, D., Karwautz, A., Nacmias, B., Granero, R., Sorbi, S., Tchanturia, K., Wagner, G., & Fernández-Aranda, F. (2008). Association of childhood eating patterns and parental attitudes to food in eating disorders: A

multicenter study. British Journal of Nutrition (doi: 10.1017/ S0007114508047752).

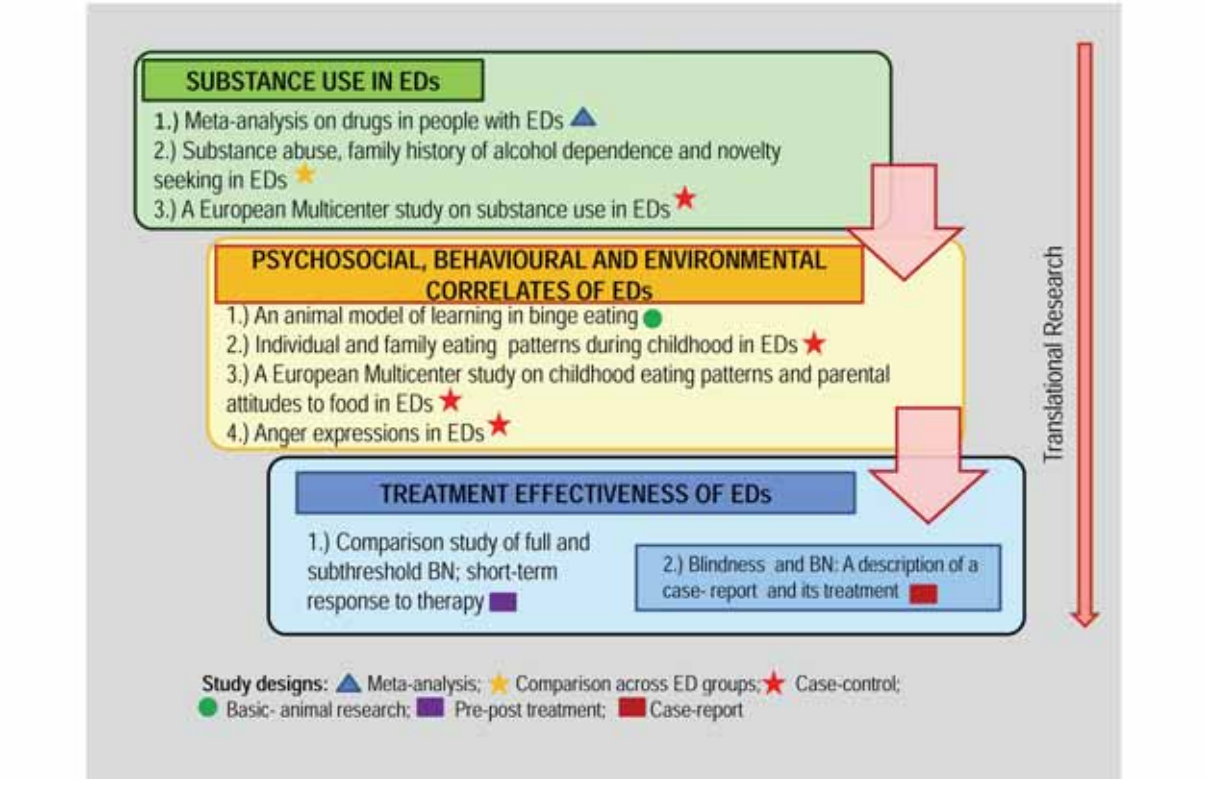
Study 7: Krug, I., Bulik, C.M., Nebot Vall-Llovera, O., Granero, R., Agüera, Z., Villarejo, C., Jiménez-Murcia, S., & Fernández-Aranda, F. (In press). Anger expression in eating disorders: clinical, psychopathological and personality correlates. Psychiatry Research (doi: 10.1080/ 1050 3300701320652).

C.) Treatment effectiveness in eating disorders

Study 8: Krug, I., Casasnovas, C., Granero, R., Martínez, C., Jiménez-Murcia, S., Bulik, C.M., Roser, G., & Fernández-Aranda, F. (2008). Comparison study of full and subthreshold bulimia nervosa: Personality, clinical characteristics, and short-term response to therapy. Psychotherapy Research, 18 (1), 37-47.

Study 9: Fernández-Aranda, F., Crepso, J.M., Jiménez-Murcia, S., **Krug, I.,** & Vallejo, J. (2006). Blindness and bulimia nervosa: A description of a case-report and its treatment. International Journal of Eating Disorders, 39, 263-265 .

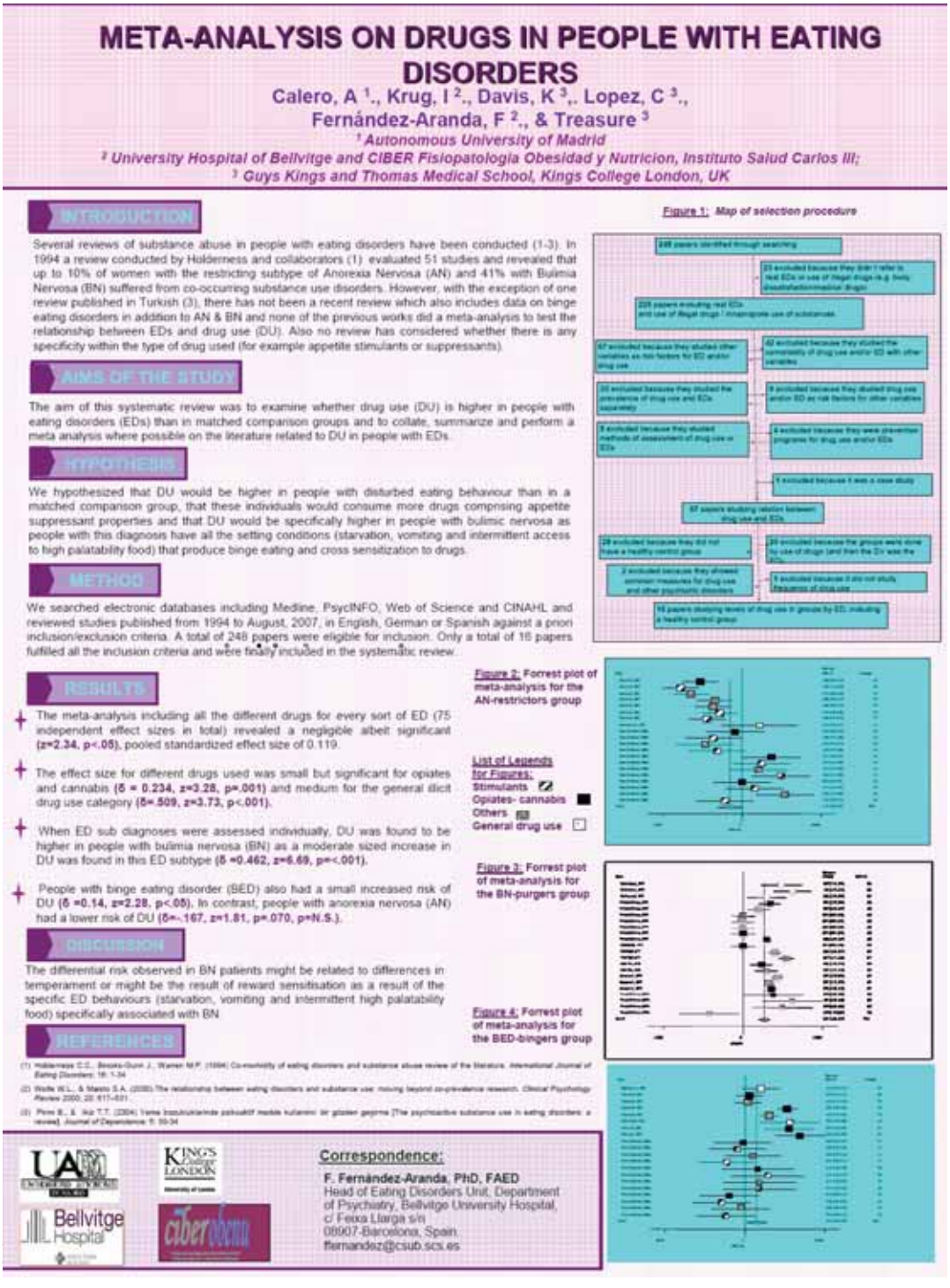
Figure 11: *Design of the Thesis*



All these studies are intended to confirm the relationship of previously identified risk factors that still have to be replicated or definitively confirmed. Furthermore, it is hoped that the present studies will provide further ground-breaking knowledge about the factors thought to be implicated in the development and maintenance of EDs. We expect that by increasing our understanding of EDs we will be able to individualize the formulation of the problem, tailor interventions more effectively to the individual and improve the outcome. Ultimately our strategic goal will be to synthesis a model of environmental risk factors for EDs that can be used in education, prevention and treatment.

8. RESULTS

8.1. Study 1



META-ANALYSIS ON DRUGS IN PEOPLE WITH EATING DISORDERS

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INTRODUCTION

Several reviews of substance abuse in people with eating disorders have been conducted (1-3). In 1994 a review conducted by Holderness and collaborators (1) evaluated 51 studies and revealed that up to 10% of women with the restricting subtype of Anorexia Nervosa (AN) and 41% with Bulimia Nervosa (BN) suffered from co-occurring substance use disorders. However, with the exception of one review published in Turkish (3), there has not been a recent review which also includes data on binge eating disorders in addition to AN & BN and none of the previous works did a meta-analysis to test the relationship between EDs and drug use (DU). Also no review has considered whether there is any specificity within the type of drug used (for example appetite stimulants or suppressants).

AIMS OF THE STUDY

The aim of this systematic review was to examine whether drug use (DU) is higher in people with eating disorders (EDs) than in matched comparison groups and to collate, summarize and perform a meta analysis where possible on the literature related to DU in people with EDs.

HYPOTHESIS

We hypothesized that DU would be higher in people with disturbed eating behaviour than in a matched comparison group, that these individuals would consume more drugs comprising appetite suppressant properties and that DU would be specifically higher in people with bulimic nervosa as people with this diagnosis have all the setting conditions (starvation, vomiting and intermittent access to high palatability food) that produce binge eating and cross sensitization to drugs.

METHOD

We searched electronic databases including Medline, PsycINFO, Web of Science and CINAHL and reviewed studies published from 1994 to August, 2007, in English, German or Spanish against a priori inclusion/exclusion criteria. A total of 248 papers were eligible for inclusion. Only a total of 16 papers fulfilled all the inclusion criteria and were finally included in the systematic review.

RESULTS

- The meta-analysis including all the different drugs for every sort of ED (75 independent effect sizes in total) revealed a negligible albeit significant **(z=2.34, p<.05)**, pooled standardized effect size of 0.119.
- The effect size for different drugs used was small but significant for opiates and cannabis **(δ = 0.234, z=3.28, p=.001)** and medium for the general illicit drug use category **(δ=.509, z=3.73, p<.001)**.
- When ED sub diagnoses were assessed individually, DU was found to be higher in people with bulimia nervosa (BN) as a moderate sized increase in DU was found in this ED subtype **(δ =0.462, z=6.69, p=<.001)**.
- People with binge eating disorder (BED) also had a small increased risk of DU **(δ =0.14, z=2.28, p<.05)**. In contrast, people with anorexia nervosa (AN) had a lower risk of DU **(δ=-.167, z=1.81, p=.070, p=N.S.)**.

DISCUSSION

The differential risk observed in BN patients might be related to differences in temperament or might be the result of reward sensitisation as a result of the specific ED behaviours (starvation, vomiting and intermittent high palatability food) specifically associated with BN

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Figure 1: Map of selection procedure

Figure 2: Forrest plot of meta-analysis for the AN-restrictors group

List of Legends for Figures.
Stimulants
Opiates- cannabis
Others
General drug use

Figure 3: Forrest plot of meta-analysis for the BN-purgers group

Figure 4: Forrest plot of meta-analysis for the BED-bingers group

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Abstract

Objective: The aim of this study was to examine whether drug use is higher in people with eating disorders and to perform a meta analysis where possible on the literature related to drug use in people with eating disorders. **Method:** We searched electronic databases (Medline, PsycINFO, Web of Science and CINAHL) and reviewed studies published from 1994 to August, 2007, in English, German or Spanish. Only a total of 16 papers fulfilled all the inclusion criteria and were finally included. **Results:** The general meta-analysis revealed a negligible albeit significant effect size (0.119, $p<.05$). Risk was found to be higher in bulimia ($\delta=0.462$, $p=<.001$), smaller in binge eating disorder ($\delta=0.14$, $p<.05$) and nonsignificant in anorexia ($\delta=-.167$, $p=.070$). **Conclusions:** The differential risk observed in patients with bulimia might be related to differences in temperament or might be the result of reward sensitisation as a result of the specific behaviours associated with bulimia.

Key words: systematic review; anorexia nervosa; bulimia nervosa; binge eating disorders; drug use

1. Introduction

During the last two decades, a body of research has indicated that substance use problems are common among women with eating disorders (EDs) [1-4]. The synthesis of the literature has not been updated since the last reviews. In 1994 a review conducted by Holderness and collaborators [5] evaluated 51 studies and revealed that up to 10 % of women with the restricting subtype of anorexia nervosa (AN) and 41% with bulimia nervosa (BN) suffered from co-occurring substance use disorders.

Wolfe and Maisto (2000) [6] also reviewed the research literature undertaken in this field in order to identify whether the hypotheses suggested to clarify the etiological correlation between EDs and substance use were confirmed by experimental evidence. With the exception of one review published in Turkish [7] there is no contemporary review on psychoactive drug use (DU) in individuals with EDs. The aim of the present study therefore was to undertake a systematic review and to use meta-analysis procedures to assess the relationship between ED and DU across all applicable studies.

Psychoactive drug use and eating disorders

As regards to DU, several studies have found that the use of a range of illicit drugs was higher in women who binged and dieted than in purely restricting AN and control individuals [8-11, 3-4, 12]. Most studies assessing DU in eating disordered individuals have however failed to specify the nature of the drug, whether it is a street drug or a prescribed medication. Differentiating the distinct classes of drugs is imperative, since some drugs such as for instance cocaine and amphetamines are known to act as appetite suppressants and are therefore employed for the purpose of weight loss, while others such as cannabis contain appetite-stimulating properties [13, 8]. The small number of studies that examined these distinct types of drugs separately demonstrated a positive relationship between dieting and bingeing (with or without purging) and stimulants, amphetamines, cocaine and psychotropic medications [1, 12, 9-10].

Animal models of drug use and eating disorders

It is probable that EDs involve a dysregulation of the hedonic system and indeed a variety of animal models have been developed to examine such a hypothesis. Animals develop unusual eating behaviors if they are exposed to some of the environmental events (starvation, stress etc) thought to be relevant to human EDs. If in addition to starvation the animals are intermittently exposed to highly palatable food then they show a pattern of behavior that resembles the binge in EDs in that they over consume these highly palatable foods [14-20]. "Binge priming" conditions include starvation, stress, high palatability foods and drainage of the stomach contents. Also not only do these animals over eat palatable food but they have also been shown to be more prone to develop addictive behaviors when exposed to alcohol and cocaine [21-22].

The hypothesis is that "binge priming" has an impact on the hedonic aspects of appetite control by producing an over sensitized reward system. Thus the theory developed to explain the results of these animal experiments is that palatable food in certain conditions may produce over sensitivity of the reward circuits as happens with drugs of abuse [23-24]. The mechanism underpinning the development of addictive behaviors is thought to be due to an imbalance in the chemical transmitters of the reward pathways. This may explain how and why change from ED symptoms becomes more difficult the longer an ED persists and fits with what is known about the developmental trajectories and how binge eating can evolve into problems with addictive behaviors.

I

In summary thus, the literature regarding the associations between EDs and DU is somewhat unclear and limited. However, it does appear that compared to restrictive AN individuals, binge eaters and BN patients are more prone to DU. Assessing the relationship between EDs and DU has both theoretical and health promotion implications since the co-occurrence of EDs and DU cause special challenges for diagnosis and treatment and have also been related to a variety of medical and psychiatric problems.

The aim of this systematic review was therefore to collate, summarise and perform a meta-analysis where possible on the literature related to DU in people with EDs. We hope that by conducting such a quantitative synthesis more convincing evidence concerning the size and direction of the relationship between DU and EDs will be obtained. More precisely, the review intended: **(1)** to study the degree of association between EDs and DU in women across all appropriate studies when compared to a healthy control condition, **(2)** to assess the relationship between different types of psychoactive drugs (stimulants, opiates-cannabis and other illicit drugs) and EDs and **(3)** to evaluate whether there were differences in the consumption of drugs across ED subdiagnoses.

We hypothesized that DU would be higher in people with disturbed eating behaviour than in a matched comparison group, that these individuals would consume more drugs comprising appetite suppressant than stimulating properties and that DU would be higher in people with bulimic features as these people have all setting conditions (starvation, vomiting and intermittent access to high palatability food) that produce binge eating and cross sensitization to drugs.

2. Methods

2.1 Literature search

We undertook a systematic literature search using four international databases: *Medline*, *PsycINFO*, *Web of Science* (*Science Citation Index Expanded, Social Sciences Citation Index, and Arts & Humanities Citation Index*) and *CINAHL*. Three people (AC, IK, KD) searched all the papers written in English, German, or Spanish which were published in peer-reviewed journals during the period between 1994 and August of 2007 inclusive. The list of search terms included: *eating disorders, eating problems, unhealthy eating, anorexia nervosa, bulimia nervosa, binge eating disorder, binge eating, purging, dieting, dietary restraint, dietary restrictions, weight concerns, body image,* and *eating attitudes*. These were linked to search terms for drugs including: *substance abuse disorders, substance use disorders, substance use, substance-related disorders, psychoactive substance use disorders, drugs,*

drug abuse, drug use, illicit drugs, psychotropics, ecstasy, MDMA, THC, stimulants, cannabis, cocaine, crack, heroin, and *opiate.* We combined each word from the "eating" set with each word from the "drug" set separately, and all these combinations of words were used combined and not combined with the term "comorbidity". In total we searched more than 400 combinations of words in each one of the databases. We also performed manual searches for the references cited in the selected papers. Once the abstracts were read, we then obtained the copies of the relevant papers.

2.2 Selection of studies

A total of 248 papers were eligible for inclusion. Papers were selected if: a) they reported the use (due to variability in measures of drug use, we considered in this review any frequency of drug use, without distinction regarding to its severity) of any sort of illegal drug use (or an innapropiate use of some legal substances) in an ED population and a comparison group (a quality criterion for the papers included in this review). We excluded papers that: a) were written in languages other than English, German, and Spanish, b) were not published in peer reviewed journals; c) reported results merely about legal drugs like alcohol, tobacco, and common medical drugs (antidepressants, anxiolytics, and antipsychotics). No restrictions were made as to the gender of participants, the age, the type of sample, or the kind of measures of DU or EDs used. Only a total of 16 papers fulfilled all the inclusion criteria and were finally included in the systematic review, 15 of them were written in English and one in Spanish. A detailed map of the selection procedure is shown in figure 1.

(INSERT FIGURE 1 HERE)

Two authors (AC, IK) reviewed the papers systematically to determine whether they fitted the inclusion criteria, one of them reviewed the papers from 1994 to 2000 and the other from 2001 to 2007 and both assigned reasons for exclusion. The decision criteria for excluded and included articles were checked by the other reviewer (IK or AC, respectively) and a third reviewer (JT).

2.3 Data extraction

All the relevant data were extracted from each paper for both the EDs and control groups. Specifically, we coded the following fields in a data extraction table: authors and year of publication, design, location, sample size, ethnicity, mean age of participants, type of sample, measures of EDs and DU, and percentage of people in each group using drugs. When necessary, we contacted the authors to obtain missing data from the published papers. In the

same paper, sometimes we found measures of the percentage of people using drugs at different time intervals. In such cases we included in the table the data that we considered more accurate and/or representative: i.e. we always selected last year or current over lifetime drug use because we considered these data more accurate (except in Telch and Stice, 1998 [25], because there is no case with current substance use), and last year over last month because we considered last year more representative data of people's substance use (readers will be able to check the selected data in each study in the table 1). Also, in some papers we found measures of drug dependence or interference with life but this data was not included, as these variables are different from drug use.

2.4 Quantitative data synthesis

Cohen's *d* effect sizes (standardized mean differences) were calculated for every comparison between groups in each study using the *Effect Size Determination Program* by Wilson (2001) [26]. Concretely, we used the procedure to calculate the effect sizes from the proportions of DU in each group, with the *Probit method* when possible and if not with the *Arcsine method*. We used Cohen's d instead of other coefficients because it is more accepted and also more frequent in the current scientific literature [27]. Cohen's effect sizes are understood as *negligible* (≥ -0.15 and <.15), *small* (≥.15 and <.40), *medium* (≥.40 and <.75), *large* ≥.75 and <1.10), *very large* (≥1.10 and <1.45) and *huge* (>1.45) [28]. Independent effect sizes were calculated for all the DU percentages included in the studies. To ensure the independence of the data for the meta-analysis, we only calculated one effect size for each kind of drug for each ED group. When the sample was divided by age or gender, effect sizes were derived for each subgroup and then the mean of effect sizes was calculated. When studies included at the same time data for specific drugs and also a general measure of DU/abuse including the mentioned specific drugs, we calculated only the effect sizes for specific drugs to ensure the independence of the data used for the meta-analysis.

The meta-analysis was carried out initially clustering all types of ED together, by a global measure of DU followed by drug subtypes, and ED subtypes. We used the program *Stata 9.1* (StataCorp, College Station, TX, USA), using the user-contributed commands for meta-analyses *metan* [29] and *metabias* [30]. Forrest plots were used to show the meta-analysis. In *metan,* we used the standard error of each study's standardized effect size which was calculated from the estimated effect and the group sizes of the two groups using the method of Cooper and Hedges (1994) [31]. Random-effect models were used [32] and also the Cochran's Q test for homogeneity to evaluate the assumption of homogeneity of true effects. This test is not very powerful with small sample sizes, so we also calculated I^2 (Q-df)/Q), a sample size independent measure of inconsistency [33]. The presence of publication bias (research with statistically significant results is potentially more likely to be submitted and published than research with non-significant results) was assessed by visual inspections of

funnel plots and then formally corroborated by Egger's [34] and Begg's adjusted rank test [35], implemented in *metabias*. These last are significance tests to identify publication bias and, as they have a low power if there are small numbers of studies, we decided to calculate both them to increase the reliability of the conclusions. Then *fill-and-trim* procedure for the correction of publication bias was used.

3. Results

3.1 Study characteristics

(INSERT TABLE 1 HERE)

Table 1 summarises the most relevant characteristics of the included studies. All studies used a cross-sectional design for the question under study. Most of the studies were from the United States (n= 5; 31.25%) and Canada (n= 5; 31.25%), four (25%) of them were carried out in different countries of Europe, one was done in Mexico and one in New Zealand. Only four studies included males, so the majority of the total sample of 42 236 people was females. The ethnicity of the participants was reported in nine out of 16 studies, with all of them including mostly white-Caucasian people.

The measures used to quantify drug use differed between studies (clinical interviews, self-questionnaires or surveys, some of them elaborated ad hoc). Some studies (n=6) described groups by DSM categories (bulimia, binge eating disorders, or anorexia), others (n= 5) used behaviours (bingers, purgers, bingers/no purgers, bingers/purgers, restrictors, diet, diet/purgers) or a combination of behaviours and attitudes (ED questionnaires; n= 5). As only 6 studies defined groups by DSM categories, we grouped together people with different severity in eating problems but always with the same type of problematic eating patterns. The comparison groups were defined in contrast to these categories. In the case of eating problems, studies also used different measures (clinical interviews, self-questionnaires, etc.).

For the analysis we grouped the problems in four categories: *anorexia/restrictors* (with four studies using groups of this category), *bulimia/purgers* (eight studies), *binge eating disorder/bingers* (six studies), and *general ED/high risk of ED* (including the last kind of studies cited above, which in total were four). Most studies (n= 14) described people with current eating problems with only two including a lifetime eating disorder history. For the purpose of this study we categorised drugs into three sub groups: 1) *stimulants of the central nervous system* (crack, cocaine, amphetamines, and ecstasy), 2) *opiates-cannabis* (cannabis/marijuana, opiates/heroin) and 3) *others* (hallucinogens, barbiturates, solvents,

sedatives, and inhalants). Furthermore, we also assessed a broad category of *general drug use*. Current or last year use/abuse was described in seven studies and lifetime consumption in nine studies.

3.2 The Meta Analysis of drug use in people with eating disorders

The meta-analysis including all the different drugs for every sort of eating disorder (75 independent effect sizes in total) revealed a negligible albeit significant (z=2.34, p<.05), pooled standardized effect size of 0.119. The data showed a high degree of heterogeneity across the studies ($X^2_{(74)}$= 1267.61, p<.001), and also the index of inconsistency, I^2, across studies reached 94.2%. Part of this heterogeneity might be due to the inclusion of populations with different diagnoses with different types of drug use.

Begg's test did not reveal the existence of publication bias (z= 0.10, p=0.92) although the visual inspection of funnel plot did as did Egger's test (t=-4.68, p<0.001). After fill-and-trim procedure, the original effect size was considerably increased from δ=.119 to δ=.428, that is, in case there was no publication bias, the effect size may be medium.

3.3 A meta-analysis of specific forms of drug use in people with eating disorders

Seven studies [36-40, 9-10] described *stimulant drug use, with a total of 25 independent comparisons.* The meta-analysis showed an effect size which was not statistically significant (δ=-.084, z=0.73, p=.46). There was evidence of heterogeneity between studies ($X^2_{(24)}$ = 492.32, p<.001) and also a high index of inconsistency across the studies (I^2= 95.1%). Contrarily to the visual inspection of funnel plot, Begg's test did not reveal publication bias (z= 0.65, p=0.51) but Egger's test did show significant bias (t=-3.40, p<0.01), which was corrected by fill-and-trim method, which increased the effect size to δ=.357 (estimated small effect size in case there was no publication bias). The forrest plots are not included in this section due to lack of space. A copy of them is available upon request.

Twelve studies described *use of opiates- cannabis* [41, 36, 42-43, 37-38, 44, 39-40, 11, 9-10] with a total of 24 comparisons in different eating disorders. The meta-analysis produced a small and significant pooled standardized effect size of 0.234 (z=3.28, p=.001). The studies were also highly heterogeneous ($X^2_{(23)}$ = 353.96, p<.001) and there was no consistency across studies, as I^2 was 93.5%. As Egger's test (t=-2.70, p<0.05) and visual inspection of funnel plot showed, there is evidence of publication bias in this topic, corroborated by the increased mean effect size of δ=.458 achieved with fill-and-trim method. Due to the extended use of cannabis in the general population, we tried to analyze the subgroup cannabis separately to

check if there were differences. We found that all the data are very similar to the group in general, with a small and significant pooled standardized mean difference of 0.246 (z=3.13, p=.002). The case mix in studies which described stimulant abuse was with a large proportion of AN-restrictors, whereas the case mix in the studies of *opiates- cannabis* included a large proportion of BN-purgers.

Seven studies described other drugs [36-37, 44, 39-40, 9-10] with a total of 17 comparisons, with non significant pooled standardized effect sizes in the whole group (δ=.047, z= 0.39, p=.69) and also considering the subgroup *hallucinogens* separately (δ=-.020, z= 0.15, p=.88). We analyzed the subgroups hallucinogens separately because it meant 11 out of 17 of the comparisons of the "other drugs" group. In both cases, the heterogeneity was high (other drugs in general, $X^2_{(16)}$ = 225.43, p<.001; hallucinogens, $X^2_{(10)}$ = 71.95, p<.001) with inconsistency across studies (other drugs in general, I^2= 92.9%; hallucinogens I^2= 86.1%). There was no evidence of publication bias according to Begg's (other drugs in general, z= -0.04, p= 1.00; hallucinogens, z= 1.09, p= .28) and Egger's (other drugs in general, t= -1.74, p= .10; hallucinogens, t= 1.80, p= .11) tests but the fill-and-trim method showed the contrary evidence in the other drugs group in general, that is, publication bias, as the effect size was increased to δ=.411 (medium estimated effect size if there was no publication bias). In the hallucinogens subgroup there was no change in effect size after fill-and-trim procedure.

Finally, in the group of *general drug use* there are five studies reporting use/abuse of any kind of drugs [45-46, 43, 25, 47] and a total number of nine independent comparisons. In this case we found a medium and significant pooled standardized effect size (δ=.509, z=3.73, p<.001). The meta-analysis revealed a high degree of heterogeneity across studies ($X^2_{(8)}$ = 93.93, p<.001) and the index of inconsistency reached 91.5%. The visual inspection of the funnel plot and Begg's (z=0.52, p=.60) and Egger's (t=0.64, p=.54) tests revealed no publication bias. Also, fill-and-trim method did not modify the original data as no trimming were performed.

3.4 A meta analysis of drug use in specific subgroups of eating disorders

Four studies analyzed drug use/abuse in the group *AN- restrictors* [39, 47, 9-10] with a total number of 20 independent comparisons. The meta-analysis showed a nonsignificant standardized effect size (δ=-.167, z= 1.81, p=.07) (see Figure 2). The heterogeneity was high ($X^2_{(19)}$ = 113.78, p<.001). There was inconsistency across studies (I^2= 83.3%). Begg's (z= 2.50, p=<0.05) and Egger's (t= 4.69, p=<.001) tests revealed publication bias. Visual inspection of the forrest plots reveals similar results across drug types but there was no change in effect size after fill-and-trim procedure.

(INSERT FIGURE 2 HERE)

In the group of *BN-purgers* there are eight studies [45-46, 36, 42-44, 40, 9] and a total number of 22 independent effect sizes. There was a medium sized combined standardized effect size of 0.462 (z=6.69, p=<.001), as shown in Figure 3. The studies were heterogeneous ($X^2_{(21)}$ = 181.57, p<.001) with no consistency across studies, as I^2 was 88.4%. Begg's (z= 0.51, p= 0.61) and Egger's test (t=-1.59, p= .13) showed no evidence of publication bias in this topic, however the fill-and-trim method increased mean effect size from δ=.462 to δ=.530.

(INSERT FIGURE 3 HERE)

There is a significant pooled standardized effect size of 0.141 (z=2.28, p<.05) in the meta-analysis performed with data from the six studies of *BED-bingers groups* [46, 25, 43-44, 9-10], including 20 independent comparisons between groups (see Figure 4). The data showed a high degree of heterogeneity across the studies ($X^2_{(19)}$ = 82.19, p<.001), and also the index of inconsistency, I^2, across studies reached 76.9. Begg's test did not reveal the existence of publication bias (z= 0.49, p= .63) and nor did Egger's test (t=-1.83, p= .08). After fill-and-trim procedure, the original effect size was increased from δ=.141 to δ=.252. There were no differences in the effect sizes in relation to the drugs used.

(INSERT FIGURE 4 HERE)

Finally, there were four studies using *general ED/high risk of ED categories* [41, 37-38, 11], with a total of 13 independent comparisons. In this group of studies the meta-analysis revealed a pooled standardized effect size of nearly 0 (δ=-.045, z=0.37; p=.07). The heterogeneity across studies was very high ($X^2_{(12)}$ = 479.22, p<.001), and also the index of inconsistency, I^2, across studies reached an extreme 97.5%. These were community studies in a younger population. Begg's (z= 3.48, p= .00) and Egger's test (t=-5.55, p= .00) revealed the existence of publication bias. After fill-and-trim procedure, the original effect size was considerably increased to δ=.407 (medium estimated effect size in case there was no publication bias).

4. Discussion

The aim of this study was to systematically estimate the direction and the strength of the association between ED and DU across published studies. Sixteen studies, comprising data on 42 236 individuals, were analysed and their outcomes merged through the computation of standardised effect sizes. The meta-analysis was carried out initially clustering all types of ED together, with a global measure of DU followed by an analysis of drug and ED subtypes. Results of this review demonstrated a significant relationship (classified as negligible) for all the different drugs for every sort of ED. As regards to different types of DU we found raised levels of *opiates-cannabis* and general illicit drugs. Finally when different ED sub diagnoses were assessed a higher prevalence of drug abuse was found particularly for BN, the prevalence was lower for BED and people with AN had lower levels of drug abuse than the healthy population.

4.1 Drug use in eating disordered individuals and healthy controls

In accordance with our first hypothesis, we found higher prevalence rates of DU in eating disordered individuals than controls. The overall findings are in accord with those found in previous reviews [5, 6, 7]. However the effect size in the present review was only negligible. Partially, this result could be attributable to the fact that most studies had been collected from community and university sites, which generally have been found to exhibit lower prevalence rates than individuals seeking treatment and therefore avoids the problem of Berkon´s bias (Berkson bias) [48].

4.2 Specific forms of drug use in people with eating disorders and controls

Our second hypothesis, which was that ED individuals would consume specifically more appetite suppressant drugs and that these might be used as part of the weight control methods was not supported. However, we revealed raised levels of *opiates-cannabis* and general illicit drugs in the ED group. These results are in accordance with some former studies [49, 13] and suggest that ED patients utilize various types of substances and not just only appetite suppressant drugs as previously anticipated. Central nervous system stimulants, such as amphetamines or cocaine, might be employed to suppress appetite. However, these drugs generally extend habitual phases of restlessness, and as a result users might turn to opiates, sleeping pills, or tranquilizers, in order to cancel out these undesired side effects [13]. However, it should be noted that the number of studies was small for each of the assessed drug categories, rendering statistical power low.

4.3 Drug use in specific subgroups of eating disorders

The results confirmed our third hypothesis, which was that DU would be higher in people with bulimia nervosa. A moderate sized increase in DU of all categories was found in this ED subtype. People with Binge Eating Disorder (BED) also revealed a small and significant increased risk of DU. In contrast, people with AN do not seem to have an increased probability for DU, as the meta-analysis showed a nonsignificant effect size. These results are in agreement with previous reviews which have indicated higher incident rates of DU in individuals with bulimic features than the general population and restrictive AN patients [5, 8]. The number of studies which split the AN group into the bulimic and restrictive AN subcategories was too small to undertake separate meaningful comparisons.

The increased risk of substance abuse in people with bulimic symptomatology (including BED) might also be related to differences in temperament such as an increased novelty seeking. This finding is also in line with other studies [50-53]. Novelty Seeking has been associated with specific neurochemical correlates, i.e., norepinephrine deregulation [54-55] and dopaminergic disturbances [56]. Impulsivity could be another candidate feature shared by the individuals who present with an ED and substance use [51-52]. Although many studies of EDs have explored the extent to which impulsivity is associated with the presence of comorbid substance use, consistent findings have not emerged. Among patients with bulimic symptomatology, however, the concept of "multi-impulsive" BN is being widely used to characterize those patients with high impulsiveness, greater comorbidity with substance use and other impulsive behaviors [57-60]. Finally another possibility is that this is an acquired change in reward sensitivity as would be predicted to occur if we are to translate from the animal models [61-62].

4.4 Limitations

The results from the present review should be considered within the context of several limitations. Firstly, there are very few studies which have examined the relationship between DU and EDs and even fewer which have included a healthy control group. Secondly, the retrospective and self-report data collection procedures employed by the majority of the studies may limit the validity and the reliability of our findings, which are subject to unreliability of individual recall and potential memory bias. Third, all studies used a cross-sectional design for the question under study which does not allow us to determine the time sequence of the different behaviours. Fourth, the included studies ascertained participants by a range of means and the technologies used to evaluate the disturbed eating behavior and DU also varied. Also, as we explained before, we had to make groups for the analyses that were heterogeneous regarding to the severity of drug use and eating problems. There was

heterogeneity in the assessed populations (ages, inpatient vs. outpatient clinical services, community sites) ED diagnoses (diagnostic criteria, disorder subtypes) and drug categories (medical or self-prescription). As we mentioned in the results section, there is high heterogeneity and inconsistency across studies, which might restrict the validity of the results Finally, since most studies were conducted with white participants from North America, no firm conclusions about the comorbidity of ED and DU in other parts of the world and distinct ethnic populations can be made.

4.5 Some preliminary clinical implications

The results of the present study also have clinical implications. First, the results emphasize the importance of assessing DU in individuals with disturbed eating behaviour, especially in those displaying bulimic symptomatology, and vice versa. It is uncertain whether treatment should be sequenced and if so in what order. However if we translate understanding from the animal models then the answer would be that treatment focused on both problems should be given conjointly.

The present review enhances our knowledge about the association between EDs and DU, but several unanswered questions remain for future studies. Longitudinal studies in naturalistic and clinical cohorts will allow us to test whether a period of BN predisposes to addictions and whether this comorbidity is a marker of disturbed reward mechanisms in the brain which may moderate or mediate treatment outcome.

In conclusion, this is the first meta-analysis examining the relationship between EDs and DU of a wide range of drug classes and ED diagnoses. This review suggests that DU is higher in individuals with EDs than healthy controls, that opiates-cannabis and general illicit drugs were the most frequently consumed drugs in the ED group and that DU was highest in people with BN. No association was found between DU and AN. One of the most striking things highlighted by this review is the marked heterogeneity of the findings. Therefore, in order to be able to comprehend more accurately the relationship between EDs and DU it is vital that researchers working in this field agree on employing standardized definitions and measures.

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Table 1: ***Characteristics of the sample***

Study	Sample		Mean age (S.D.) or age range	Type of sample	Measure of ED	Measure of drugs	% of drug use
	Group	N					
Bushnell *et al.* (1994)	Clinical BN	25 f	M= 23.5 (4.9)	Clinical	Diagnosis Interview Schedule (DIS), version 3A	Diagnosis Interview Schedule (DIS), version 3A	Drug abuse. Lifetime: 32%
	Community BN	20 f	M= 27.2 (6.3)	Community			Drug abuse. Lifetime: 24%
	HC	777 f	18-44 years	Community			Drug abuse. Lifetime: 6%
Baptista *et al.* (1996)	BN	22 f	M= 25.3 (6.6)	University	Self-questionnaire (not specified. Available upon request)	Self-questionnaire (not specified. Available upon request)	Illicit drugs. Lifetime: 13.6%
	BED	97 f	M= 27.8 (8.2)	University			Illicit drugs. Lifetime: 7.7%
	HC	439 f	M= 26.1 (6.5)	University			Illicit drugs. Lifetime: 5.3%
Neumark-Sztainer *et al.* (1996)	Unhealthy weight loss beh.	6th grade: 254 m/f; 9th grade: 427 m/f; 12th grade: 350 m/f	Early to late adolescence	Community	Minnesota student survey	Minnesota student survey	Marijuana. Current: 6th grade=11.9%; 9th grade= 21.1%; 12th grade= 24.6%
	HC	6th grade: 285 m/f; 9th grade: 1556 m/f; 12th grade: 1642 m/f	Early to late adolescence	Community			Marijuana. Current: 6th grade= 2.9%; 9th grade= 4.9%; 12th grade= 8.4%
Welch & Fairburn (1996)	BN	102 f	M= 23.7 (4.9)	Community	Eating Disorder Examination (EDE) interview	Semistructured interview designed at hoc	Last month (>0): Cannabis=18.63%; Amphetamine=2.94%; Solvents= 0%; Cocaine= 0%; Crack= 0%; Opiates= 0%; Other illicit drugs= 1.96%
	HC	204 f	matched	Community			Last month (>0): Cannabis= 6.86%; Amphetamine= 0%; Solvents= 0%; Cocaine= 0%; Crack= 0%; Opiates= 0%; Other illicit drugs= 0.49%
Devaud *et al.* (1998)*	High PEC	76 f	15-20 years	Community	Swiss Multicenter Adolescent Health Survey (SMASH)	Swiss Multicenter Adolescent Health Survey (SMASH)	Cannabis. Lifetime: 8%
	HC	371 f	15-20 years	Community			Cannabis. Lifetime: 8%
Telch & Stice (1998)	BED	61 f	M= 43.5 (8.7)	Community	Questionnaire on Eating and Weigh Patterns (QEWP); BES; Eating Disorders Examination- Questionnaire (EDE-Q); Three-Factor Eating Questionnaire (TFEQ; measure of height and weight	Structured Clinical Interview (SCID) for DSM-III-R	Substance abuse. Lifetime: 9%
	HC	60 f	M= 45.0 (10.1)	Community			Substance abuse. Lifetime: 3%

f: females/m: males; BN: bulimia nervosa; AN: anorexia nervosa; BED: binge eating disorder; HC: healthy controls; ED: eating disorder

* Only included PEC (problematic eating conduct. BN/BED), not WIC dimension (weight and image concern); ** Only included data about females, not specified data about males in the sample

*** Only data from self-report of former AN and control group were analyzed, but not the data from parents; **** In these studies we only analyze the data from the first analysis, as the groups were selected based on specific eating disorders behaviours

Study	Sample		Mean age (S.D.) or age range	Type of sample	Measure of ED	Measure of drugs	% of drug use
	Group	N[a]					
Ross & Ivis (1999)	Past BED	62 m	M= 15.2 (2.2)	Community	Questionnaire designed at hoc	Questionnaire designed at hoc	Last year: Cannabis= 17.7%; Other drugs= 11.1%
		111 f					Last year: Cannabis= 25.0%; Other drugs= 19.8%
	Binge/No purgers	155 m	M= 15.2 (1.9)	Community			Last year: Cannabis= 39.0%; Other drugs= 23.9%
		195 f					Last year: Cannabis= 33.7%; Other drugs= 19.5%
	Binge/Purgers	46 m	M= 15.4 (1.8)	Community			Last year: Cannabis= 43.5%; Other drugs= 39.1%
		167 f					Last year: Cannabis= 44.6%; Other drugs= 51.2%
	HC	625 m	M= 14.8 (2.2)	Community			Last year: Cannabis= 21.6%; Other drugs= 15.1%
		558 f					Last year: Cannabis= 17.8%; Other drugs= 13.4%
Gutiérrez *et al.* (2001)	Risk of ED	143 f	M= 14.7 (1.7)	Community	Survey on Drugs and Alcohol Use Prevalence in student population in the Federal District	Survey on Drugs and Alcohol Use Prevalence in student population in the Federal District	Lifetime: Cocaine= 2.1%; Inhalants= 2.8%; Amphetamines/Stimulants= 0.7%; Marijuana= 3.5%; Sedatives= 2.1%; Heroin= 0%; Crack= 0%; Hallucinogens= 1.4%
	HC	143 f		Community			Lifetime: Cocaine= 8.4%; Inhalants= 7.7%; Amphetamines/Stimulants= 7.7%; Marijuana= 6.3%; Sedatives= 3.5%; Heroin= 2.8%; Crack= 0.7%; Hallucinogens= 0.7%
Lock *et al.* (2001)	Risk of ED	221 m	Males, M= 16 (1.17); females M= 15.86 (1.15)	Community	Juvenile Wellness and Health Survey-76 (JWHS-76)	Juvenile Wellness and Health Survey-76 (JWHS-76)	Lifetime: Marijuana= 34.3%; Heroin= 13.7%; Cocaine= 4.2%
		163 f					Lifetime: Marijuana= 44.9%; Heroin= 21.3%; Cocaine= 5.1%
	HC	581 m		Community			Lifetime: Marijuana= 30.3%; Heroin= 9.7%; Cocaine= 2.0%
		500 f					Lifetime: Marijuana= 25.9%; Heroin= 8.4%; Cocaine= 1.2%
Dunn *et al.* (2002) ***	BN	68 f	M= 21.3 (5.22)	University	Eating Disorder Diagnostic Scale (EDDS)	Customary Drinking and Drug Use Record (CDDR)	Lifetime: Marijuana= 64.7%; Barbiturates= 23.5%
	BED	45 f		University			Lifetime: Marijuana= 68.9%; Opiates= 33.3%
	HC	1749 f		University			Lifetime: Marijuana= 48.7%; Opiates= 13.8%; Barbiturates= 11.0%
Stock *et al.* (2002)	Restrictors	63 f	M= 15.1 12-17 years	Clinical	Clinical interview	Questionnaire from the DUAOS survey	Last year: Cannabis= 12.7%; Stimulants= 1.7%; LSD= 1.7%; PCP= 0%; Hallucinogens= 6.7%; Cocaine: 1.7%; Ecstasy= 1.7%
	HC	4894 f	-	Community			Last year: Cannabis=28.8%Stimulants10.2%; LSD= 7.9%; PCP= 3.5%; Hallucinogens= 13.7%; Cocaine: 3.5%; Ecstasy= 5.1%

Study	Sample		Mean age (S.D.) or age range	Type of sample	Measure of ED	Measure of drugs	% of drug use
	Group	N[a]					
Cance *et al.* (2005)	Purgers	429 f	M= 14.48 12-17 years	Community	Clinical interview (National Household Survey on Drug Abuse)	Clinical interview (National Household Survey on Drug Abuse)	Last year: Ecstasy= 10.4%; Inhalants: 9.1%; Marijuana= 28%
	HC	3863 f		Community			Last year: Ecstasy= 2.2%; Inhalants: 2.9%; Marijuana= 11.4%
Halvorsen *et al.* (2005)[*][**]	Former AN	47 f	M= 23.1 (3.4)	Clinical	Eating Disorder Examination (EDE)	Young Adult Self-Report (YARS) or Youth Self-Report (YSR)	Drug use. Last 6 months: 14.89%
	HC	20 m/f	M= 24.4 (5.5)	Community			Drug use. Last 6 months: 10%
Piran & Gadalla(2007)	Risk of ED	15-24 years: 122 f; 25-44 years: 222 f; >44 years: 229 f	-	Community	Clinical interview	Canada's Alcohol and Other Drugs Survey (CADS)	Cannabis. Last year: 15-24 years= 40.0%; 25-44 years= 15.7%; >44 years= 1.5%
	HC	15-24 years: 3093 f; 25-44 years: 7270 f; >44 years: 9168 f	-	Community			Cannabis. Last year: 15-24 years= 25.4%; 25-44 years= 8.7%; >44 years= 1.7%
Piran & Robinson (2006a)[*][**][***]	Bingers	43 f	M= 21.8 (2.25)	Community	Women's Health Survey	Women's Health Survey	Lifetime: Marijuana= 56%; Cocaine= 12%; Hallucinogens/Heroin= 30%; Stimulants/ Amphetamines= 9%
	Severe bingers	24 f		Community			Lifetime: Marijuana= 63%; Cocaine= 21%; Hallucinogens/Heroin= 33%; Stimulants/ Amphetamines= 17%
	Severe diet	30 f		Community			Lifetime: Marijuana= 53%; Cocaine= 7%; Hallucinogens/Heroin= 13%; Stimulants/Amphetamines= 7%
	Diet/Purgers	29 f		Community			Lifetime: Marijuana= 72%; Cocaine= 21%; Hallucinogens/Heroin= 35%; Stimulants/ Amphetamines= 28%
	Purgers	10 f		Community			Lifetime: Marijuana= 80%; Cocaine= 50%; Hallucinogens/Heroin= 60%; Stimulants/ Amphetamines= 0%
	HC	139 f		Community			Lifetime: Marijuana= 57%; Cocaine= 14%; Hallucinogens/Heroin= 27%; Stimulants/ Amphetamines= 13%
Piran & Robinson (2006b)[*][**][***]	Bingers	38 f	M= 20.84 (1.60)	University	Women's Health Survey	Women's Health Survey	Lifetime: Marijuana= 34%; Cocaine= 0%; Hallucinogens/Heroin= 11%; Stimulants/ Amphetamines= 3%
	Severe diet	29 f		University			Lifetime: Marijuana= 41%; Cocaine= 3%; Hallucinogens/Heroin= 28%; Stimulants/ Amphetamines= 3%
	HC	174 f		University			Lifetime: Marijuana= 41%; Cocaine= 2%; Hallucinogens/Heroin= 12%; Stimulants/ Amphetamines= 5%

Figure 1: *Map of selection procedure*

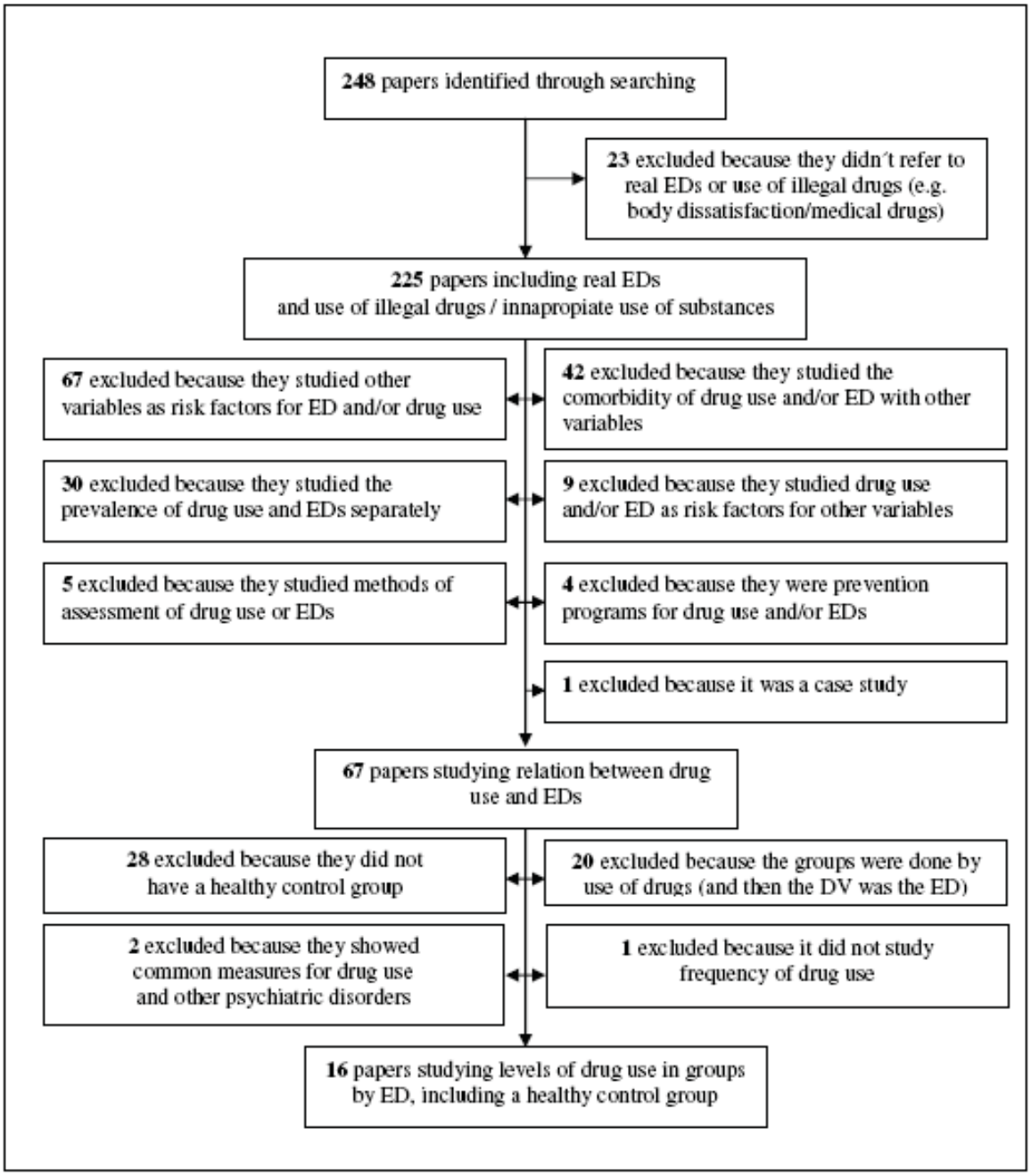


Figure 2. ***Forrest plot of meta-analysis for the AN-restrictors group***

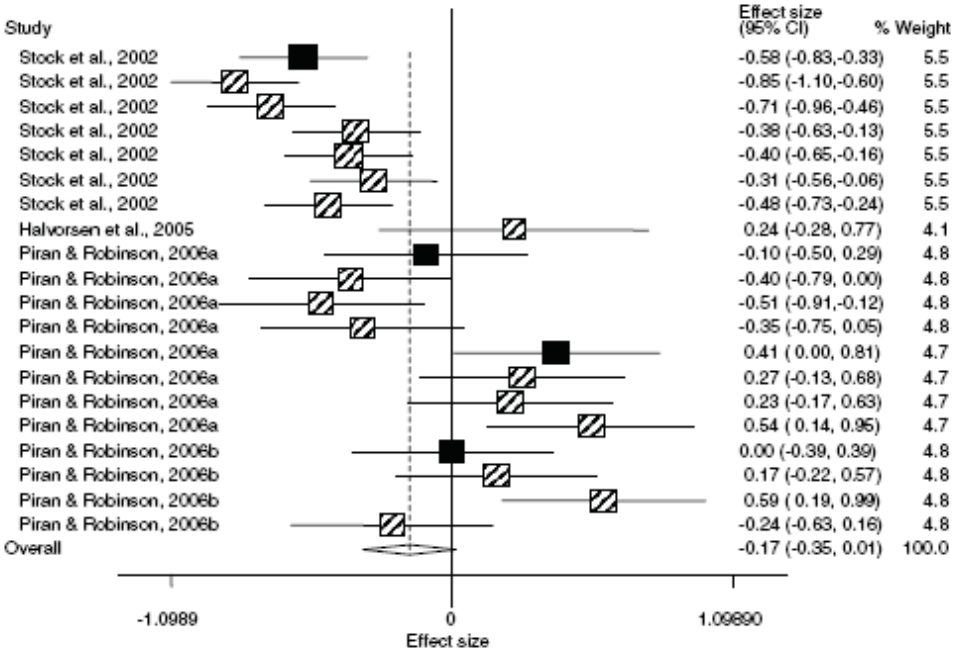


Figure 3. ***Forrest plot of meta-analysis for the BN-purgers group***

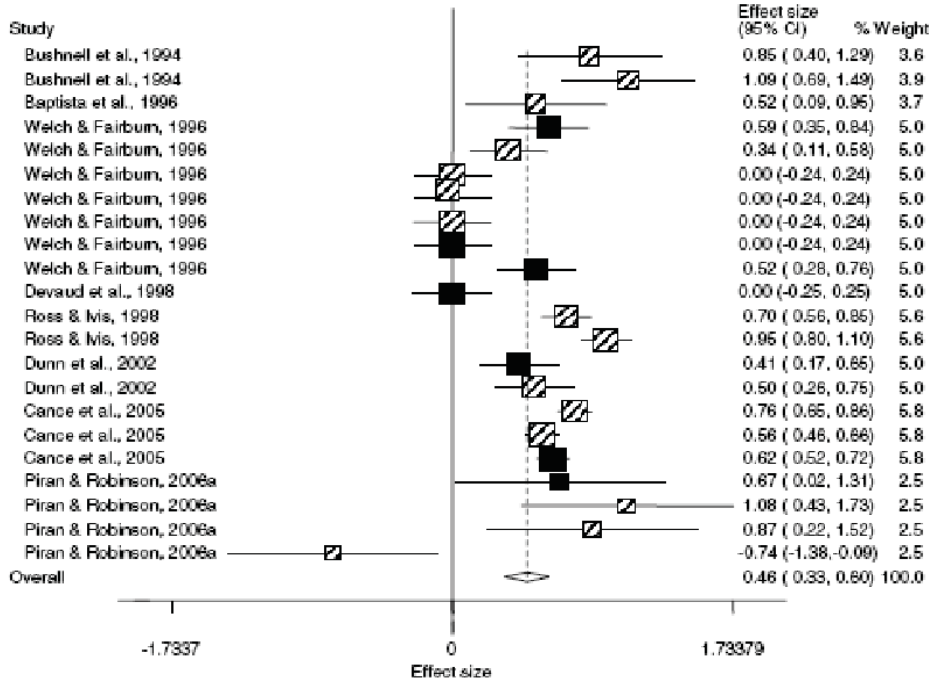
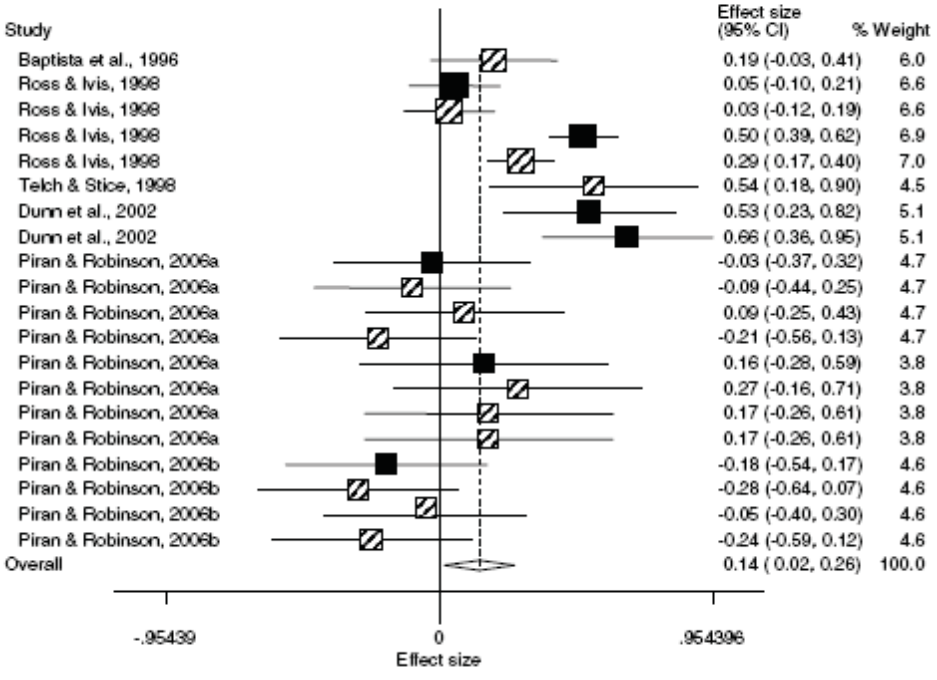


Figure 4. ***Forrest plot of meta-analysis for the BED-bingers group***



8.2. Study 2

LIFETIME SUBSTANCE ABUSE, FAMILY HISTORY OF ALCOHOL DEPENDENCE AND NOVELTY SEEKING IN EATING DISORDERS: A COMPARISON STUDY OF EATING DISORDERS SUBGROUPS.

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INTRODUCTION

Reviews of the literature on co-occuring substance use in eating disorders (ED) indicate that individuals with bulimic features are generally more likely to abuse alcohol and other drugs than individuals suffering from the restricting subtype of anorexia nervosa (AN) (1). In AN women with bulimic symptoms, the occurrence of substance abuse seems to be analogous to or surpass that in patients with BN (2). Variations in patterns of familial liability (3) and in novelty seeking (4) may account for these differences.

OBJECTIVES

To assess lifetime substance abuse, family history of alcohol dependence, and novelty seeking in three different ED groups [Anorexia Nervosa- Restrictive; Anorexia Nervosa-Binge Eating/ Purging and Anorexia Nervosa who cross over to BN].

HYPOTHESES

- AN patients with bulimic symptoms when underweight have greater prevalence of substance abuse than those with restrictive symptomatology and those who cross over to BN after weight restoration.
- These patients report a greater family history of alcohol dependence and higher novelty seeking.
- Higher novelty seeking is associated with substance use.
- Family history of alcohol dependence predicts novelty seeking.

METHOD

PARTICIPANTS

N=371 females: 130 AN-R, 119 AN-BP and 122 AN-CROSS. Participants were diagnosed according to DSM-IV-TR criteria.

ASSESSMENT

- Lifetime substance abuse and family history of alcohol dependence DSM IV-SCID.
- Novelty Seeking (NS): Temperament and Character Inventory-Revised (TCI-R).

STATISTICAL ANALYSIS

SPSS

- ANOVA and the chi-square tes to compare the continuous and discrete variables in the study groups.
- Logistic regression model to evaluate the extent to which novelty seeking (independent variable) could predict the presence or not of lifetime substance abuse (dependent variable).
- Linear regression to analyze the associations among age of onset, maximum BMI, ED diagnosis, family history of alcohol dependence, education and total novelty seeking.

RESULTS

- The AN-R individuals exhibited significantly less lifetime substance abuse and family history of alcohol dependence compared with the AN-BP and AN-Cross patients.
- The mean score on NS was significantly higher in the AN-CROSS group than in the AN-R and AN-BP groups.
- NS was significantly associated with substance abuse in patients with bulimic features namely AN-BP and AN-Cross, but not in restricting AN individuals (OR=1.034, 95% CI=1.01-1.06, p=0.002).
- Family history of alcohol dependence was not significantly associated with NS (B = 3.6, 95% CI=-0.59-7.78, p= 0.09).

Table 1: **Sociodemographic variables by ED diagnostic subtype**

		AN-R (N=130)	AN-BP (N=136)	AN-Cross (N=122)	p	Eating Disorder Group Difference
Marital Status	Single	84.6 %	80.2 %	43 %	0.001	AN-Cross>AN-R>AN-BP
Education	Primary	28.6 %	21.3 %	27.1 %	0.37	N.S.
	Secondary	34.1 %	39.3 %	38.4 %		
	University	23.3 %	16.8 %	11.9 %		
Employment Status	Employed	31.1 %	30.3 %	47.4 %	0.02	AN-Cross>AN-R>AN-BP
	Unemployed	12.6 %	21.9 %	12.1 %		AN-BP>AN-Cross>AN-R
	Student	34.1 %	23.7 %	27.8 %		AN-R>AN-Cross>AN-BP
Age	Mean (SD)	24.32 (8.18)	24.85 (7.59)	27.38 (7.80)	0.22	N.S.

Note: AN-R =Anorexia Nervosa Restrictive Subtype; AN-BP = Anorexia Nervosa Purging/Bingeing Subtype; AN-Cross = Anorexia Nervosa patients who crossed over to Bulimia Nervosa.

Figure 1: **Prevalence of substance abuse and family history of alcohol dependence across ED diagnoses**

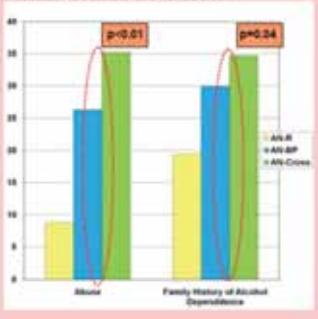
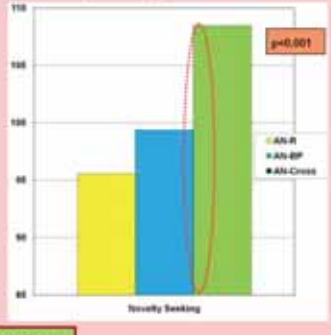


Figure 2: **Differences in the Novelty Seeking mean scores across ED diagnostic subtype**



DISCUSSION

The presence of a lifetime history of substance abuse may be particularly prevalent in patients with bulimic characteristics with high novelty seeking. EDs and substance abuse may represent expressions of a predisposition to addictive behaviour possibly related to the genetically influenced trait of novelty seeking.

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LIFETIME SUBSTANCE ABUSE, FAMILY HISTORY OF ALCOHOL ABUSE/DEPENDENCE AND NOVELTY SEEKING IN EATING DISORDERS: A COMPARISON STUDY OF EATING DISORDERS SUBGROUPS.

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Field to which the manuscript is being submitted: General topics in psychiatry and related fields.

ABSTRACT

Objective: To assess lifetime substance abuse, family history of alcohol abuse/dependence, and novelty seeking in three different eating disorder groups [Anorexia Nervosa-Restrictive, Anorexia Nervosa-Binge Eating/Purging and Anorexia Nervosa who crossed over to Bulimia Nervosa]. **Method:** A total sample of 371 eating disorder patients participated in the current study. Assessment measures included the prevalence of substance abuse and family history of alcohol abuse/dependence as well as the novelty seeking subscale of the Temperament and Character Inventory- Revised. **Results:** Significant differences across groups were detected for lifetime substance abuse, with Anorexia Nervosa-Restrictive individuals exhibiting a significant lower prevalence than the Anorexia Nervosa who cross over to Bulimia Nervosa and Anorexia Nervosa- Binge Eating/Purging patients ($p<0.01$). For family history of alcohol abuse/dependence the same pattern was observed ($p=0.04$). Novelty seeking was associated with substance abuse ($p=0.002$), with the Anorexia Nervosa who crossed over to Bulimia Nervosa group exhibiting significantly higher scores on the novelty seeking scale than the other two groups ($p<0.001$). However, family history of alcohol abuse/dependence was not related to novelty seeking ($p=0.092$). **Conclusion:** Lifetime substance abuse appears to be more prevalent in Anorexia Nervosa patients with bulimic features. Higher novelty seeking scores may be associated with diagnosis crossover.

Key words: eating disorders, anorexia nervosa, bulimia nervosa, personality, substance abuse

1. Introduction

Reviews of the literature on co-occurring substance use in eating disorders (ED) indicate that individuals with bulimic features are generally more likely to abuse alcohol and other drugs than individuals suffering from the restricting subtype of anorexia nervosa (AN) (1-5), although this observation is not universal at intake diagnosis (6-7).

As previous studies have suggested this disparity across ED subtypes may reflect variations in patterns of familial liability to EDs (8-10). In relation to AN, increased occurrence of substance use disorders have been reported among relatives of non-substance abusing underweight AN individuals with binge eating compared to restricting subtype AN and to weight recovered AN patients who subsequently cross over to Bulimia Nervosa (BN) (11-12).

Previous studies have shown that especially a predisposition to alcoholism seems to be genetically transmitted (13). In addition, other studies have documented higher rates of comorbid and familial alcohol and substance use disorders in women with bulimia and their family members (14-16).

A recent review on the sensitivity to reward and punishment in EDs has advocated that specific personality traits such as impulsivity and sensation seeking may predispose a person both to EDs and to substance abuse (17). In particular, this review showed that patients with bulimic symptoms exhibit higher scores on sensation seeking, than individuals with restricting AN and controls which has also been supported by recent studies (e.g., 18).

According to Cloninger (19), temperament is largely heritable. Research on the genetic background of Cloninger's temperament model has been most active in relation to novelty seeking (20). It has been observed that maternal and paternal frequency of alcohol intake was associated with offspring temperament and character dimensions, particularly novelty seeking (21).

In summary, evidence exists that even though substance abuse is infrequent in individuals with the restricting subtype of AN, in AN women with bulimic symptoms, the occurrence of substance abuse seems to be analogous to or surpass that in patients with BN. Variations in patterns of familial liability and in novelty seeking may account for these differences but have not previously been assessed in AN patients and individuals who subsequently cross over to BN.

Accordingly, we hypothesize that patients who exhibit bulimic symptoms when underweight will have greater prevalence of substance abuse than those who have purely restrictive symptomatology and those who cross over to BN after weight restoration. Furthermore, we hypothesize that these patients will also report a greater family history of alcohol dependence. Finally we assumed that higher novelty seeking would be associated with

substance use and that family history of alcohol abuse/dependence would predict novelty seeking.

2. Methods

2.1. Participants

A total sample of 371 female eating disordered patients participated in the current study [130 AN-R - Anorexia Nervosa-Restrictive, 119 AN-BP -Anorexia Nervosa-Binge Eating/Purging and 122 AN-CROSS - Anorexia Nervosa who crossed over to Bulimia Nervosa]. Participants were consecutive referrals for assessment and treatment at the Eating Disorder Unit at the Department of Psychiatry of the University Hospital of Bellvitge in Barcelona. All participants were diagnosed according to DSM-IV-TR criteria (22). The mean age for the total sample was 24.77 years (SD=5.54).

2.2. Assessment

2.1.1. Evaluation of lifetime substance abuse and family history of alcohol abuse/dependence

The patients were assessed by a structured clinical face to face interview modeled after the Structured Clinical Interview for DSM IV-SCID I (23), covering ED and lifetime presence of impulsive behaviors (namely alcohol and drug abuse, comorbid impulse control disorders and suicide attempts) and family antecedents of alcohol abuse/dependence.

2.1.2. Novelty Seeking subscale of the Temperament and Character Inventory-Revised (TCI-R) (24)

The Novelty Seeking subscale of the TCI-R (24) is a 4-item, five point Likert scale, reliable and valid subscale that measures one of the four temperament domains of the TCI-R. The performance on the Spanish version of the revised TCI-R version (25) showed an internal consistency (coefficient alpha) of 0.87.

2.3. Procedure

Experienced psychologists and psychiatrists completed the anamnesis during two structured face to face interviews before any psychological or pharmacological treatment was implemented. In addition to the clinical interview further demographic information was obtained through self-report questionnaires. All patients gave their informed consent to participate in the study and patient anonymity was preserved, the protocol of which was approved by our institutional Ethics Committee.

2.4. Statistical analysis

The statistical analysis was conducted with statistical package SPSS, version 15.0. All significance tests were two-tailed. One-way analysis of variance (ANOVA) and chi-square tests were applied to compare the continuous and discrete variables in the study groups. For the ANOVA analyses, Bonferroni post hoc comparisons were conducted to assess which groups differed and for the chi-square test Holmes analysis was carried out to correct for multiple comparisons.

Logistic regression model, employing ENTER procedure, was employed to evaluate the extent to which novelty seeking (independent variable) could predict the presence or absence of lifetime substance abuse (dependent variable). The model was adjusted by ED diagnosis, age of onset, BMI and education with the AN-R group entered as the reference group. The model's ability to discriminate between groups was assessed with the area under the receiver operator curve (ROC). The model's calibration was examined using the Hosmer and Lemeshow test. Finally, Nagelkerke R^2 was used to estimate how much variance was accounted for in the model.

The associations among age of onset, maximum BMI, ED diagnosis, family history of alcohol abuse/dependence, education and total novelty seeking was analyzed by linear regression. Total novelty seeking, a continuous variable, was used as the dependent variable, while the remaining variables were employed as independent variables. No interaction terms were included since none of the multiplicative interactions were significant after Bonferroni adjustment.

3. Results

3.1. Sociodemographic and clinical variables

Table 1 details the sociodemographic and clinical information of the three ED subgroups AN-R, AN-BP and AN-Cross. Groups did not differ on education, current age or number of previous treatments. Statistically significant differences across the groups emerged for marital and employment status, age of onset, duration of the disorder, current, minimum, and maximum BMI as well as weekly frequency of binge eating and vomiting episodes and laxative use.

3.2. Prevalence of lifetime substance abuse and family history of alcohol dependence by eating disorder subtype.

Results presented in table 1 also indicate that groups differed in the observed frequency of lifetime substance abuse, with the AN-R individuals exhibiting significantly less lifetime substance abuse (n=9, 8.8%) compared with the AN-BP (n=26, 26.3%) and AN-Cross patients (n=43, 35.2%) ($p<0.001$). For family history of alcohol abuse/dependence the same pattern of findings was observed (AN-R: n=19, 19.4%; AN-BP: n=29, 29.9%; AN-Cross: n=42, 34.7%, p=0.04). Participants with AN-BP and AN-Cross were similar, and reported a significantly higher prevalence of family history of alcohol abuse/dependence than participants with AN-R. Significantly higher mean TCI-R novelty-seeking scores were obtained for the AN-Cross group than for the AN-R and AN-BP groups ($p<0.001$).

{Insert TABL E 1 about here.}

3.3. The relation between novelty seeking, lifetime substance abuse and family history of alcohol abuse/dependence

Results from the logistic regression analysis indicated that novelty seeking was significantly associated with substance abuse in patients with bulimic features, namely AN-BP and AN-Cross, but not in restricting AN individuals (OR=1.034, 95% CI=1.01-1.06, p=0.002). Moreover, the adjustment of the model was correct (values p =0.767 in the Hosmer and Lemershow tests). The total variance accounted for in the model was 16.6 %. Furthermore, the model was able to discriminate among the groups since the area under the receiver operator curve was 0.505. Finally we found that family history of alcohol dependence was not significantly associated with novelty seeking scores in the patient (β=3.6, 95% CI= -0.59-7.78; p=0.09). The total variance accounted for in the model was only 3.4 %.

{Insert TABL E 2 about here.}

4. Discussion

Our first hypothesis was only partially supported since we found that both the AN-Cross and the AN-BP group exhibited the highest prevalence for substance use and family history of alcohol dependence. However, we were not able to reveal that the AN-BP group exhibited higher values than the AN-Cross group. Furthermore our second hypotheses was also only to some extent confirmed. Novelty seeking was significantly associated with substance use in individuals with bulimic features, but no differences were observed for AN-BP and AN-Cross groups. On the other hand, AN-Cross showed significantly higher scores on novelty seeking when compared to the AN-R and AN-BP groups. Finally, family history of alcohol abuse/dependence was not associated with the patients' novelty seeking scores.

Our finding that the AN-BP and AN-Cross patients presented significantly higher prevalence of substance use than the AN-R patients confirms previous research (1, 3, 12, 26) in which those individuals with BN or with a history of bulimic symptoms in the course of AN report higher prevalence of substance use disorders. Given that substance abuse and dependence are correlated with worse outcomes from EDs (27) and greater comorbidity (12) it is germane that we attempt to identify characteristics or personality features associated with alcohol and drug problems in this patient population.

In relation to family and genetic factors, our findings that family history of alcohol abuse/dependence was significantly lower in the AN-R than in the AN-BP and AN-Cross groups is also in line with earlier studies (8,9).

The frequent association of substance use disorders and EDs has led some authors to consider this comorbidity as part of an overall addictive dimension of personality (1,28,29). In addition, impulsivity has been associated to both bulimic behaviors and substance use problems (30).

Finally, our results concerning the link between novelty seeking and substance use in the AN-BP and AN-Cross but not the AN-R group concurs with recent papers (5, 17, 31). The elevated novelty seeking scores found in our bulimic groups (AN-BP and AN-Cross) may be related to the emergence of binge eating at some point during the course of the eating disturbance (2, 18, 32).

The use of behavioral models of binge eating and other feeding protocols is beginning to clarify the overlap between binge eating and substance use behaviors. Animal models have shown that neural signals relevant to binge eating are comparable with those involved in substance abuse (33). For example, animal studies have shown increased self administration of ethanol, alcohol and cocaine (34-36) under conditions of food deprivation.

In humans, it's possible that individuals with higher baseline novelty seeking may also become more vulnerable to substance abuse under conditions of food deprivation such as that seen in AN and BN, be it long term starvation or the fluctuating availability associated with the binge/starve pattern of BN. Accordingly, there is evidence suggesting that food restriction induces changes in dopaminergic transmission including hyper responsiveness to novelty and environmental stimuli that signal opportunity for drive reduction (37).Individual differences in the magnitude of this response have been found to correlate with rewarding effects of the drugs and the personality trait of novelty seeking (37).

When we looked at novelty seeking scores and compared them among all three groups, we observed that AN-Cross had significantly higher scores than the two other groups: AN-R had the lowest whereas AN-BP had intermediate scores. Novelty seeking may be associated with substance abuse in those with bulimic features but may also be related to diagnostic instability. Other studies have pointed to personality traits as factors that might mediate eating disorder diagnostic crossover (38).

Treatment approaches addressing both conditions may therefore eventually produce superior effectiveness than those that concentrate exclusively on the disorder for which the individual sought treatment. This is especially so if the factors that prompt both the EDs and substance abuse behaviors are common (i.e. underlying novelty seeking) and if the behaviors are interrelated (e.g. food deprivation increasing the risk of substance use, and substance use disinhibiting binge eating).

The present results should be considered within the context of several limitations. First, the retrospective and self-report data collection procedures may limit the validity and the reliability of our findings. Second, the cross-sectional design does not allow us to determine causality of the variables assessed. Third, the risk of spurious results due to comorbidity of index patients with Axis I and Axis II diagnoses should be considered. Fourth, we were not able to assess family history of other substances than alcohol abuse/dependence. Finally, since in our study the novelty seeking subscale of the TCI-R was measured after the diagnosis of the ED, the measurement in the AN groups was performed under food deprivation and hence it is difficult to discuss baseline novelty seeking in this study design. Balancing these shortcomings was the fact that we employed a large sample size of ED patients and that the sample sizes of each of the sub-diagnoses were equivalent.

Several unanswered questions remain for future study. Research in this area could improve by exploring longitudinal patterns of temporal association. Secondly, even though bingeing and purging behaviors in AN often take place concurrently, it has been proposed that purging, rather than bingeing is most strongly associated with severity of psychopathology. Therefore future research should assess whether comorbid substance use differs among restrictive individuals with exclusively bingeing or purging symptom patterns.

In summary, the presence of a lifetime history of substance use may be particularly prevalent in patients with bulimic characteristics with high novelty seeking. EDs and substance abuse may represent expressions of a fundamental predisposition to addictive behavior possibly related to the genetically influenced trait of novelty seeking. Higher novelty seeking may be associated with diagnostic cross over from AN to BN.

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Table 1: Sociodemographic and clinical variables by eating disorder diagnostic subtype

		AN-R (N=130)	AN-BP (N=119)	AN-Cross (N=122)	P	Eating Disorder Group Differences
Sociodemographics						
Marital Status	*Single*	66.6 %	60.2 %	43 %	0.002	AN-Cross<AN-R=AN-BP
Education	*Primary* *Secondary* *University*	20.8 % 54.1 % 23.3 %	21.5 % 58.0 % 16.8 %	27.1 % 58.4 % 11.9 %	0.33	N.S
Employment Status	*Employed* *Unemployed* *Student*	31.1 % 12.6 % 34.5 %	30.5 % 21.9 % 25.7 %	47.4 % 12.1 % 27.6 %	0.02	AN-Cross>AN-R=AN-BP AN-BP>AN-Cross=AN-R AN-R>AN-Cross=AN-BP
Age	Mean (SD)	24.12 (6.19)	24.85 (5.59)	25.38 (5.36)	0.22	N.S
Clinical features						
Age of onset	Mean (SD)	19.97 (4.63)	18.44 (4.42)	17.48 (4.37)	<0.001	AN-R>AN-BP=AN-Cross
Duration of the disorder	Mean (SD)	3.99 (3.88)	6.47 (4.94)	8.16 (5.11)	<0.001	AN-R<AN-BP<AN-Cross
Number of previous treatments	Mean (SD)	0.96 (1.16)	1.38 (1.51)	1.07 (1.45)	0.10	N.S
Current BMI	Mean (SD)	16.16 (1.88)	16.55 (1.91)	20.90 (2.47)	<0.001	AN Cross> AN-R=AN-BP
Maximum BMI	Mean (SD)	21.67 (2.88)	22.58 (3.14)	24.13 (3.57)	<0.001	AN Cross> AN-R=AN-BP
Minimum BMI	Mean (SD)	15.12 (1.64)	15.33 (1.72)	16.45 (1.46)	<0.001	AN Cross>AN-R=AN-BP
Weekly freq. of binges	Mean (SD)	0	1.94 (4.08)	8.41 (8.00)	<0.001	AN-R<AN-BP<AN-Cross
Weekly freq. of vomits	Mean (SD)	0	5.13 (6.49)	9.17 (9.56)	<0.001	An-R<An-BP<AN-Cross
Weekly freq. of laxatives	Mean (SD)	0	7.37 (14.42)	7.06 (29.13)	0.01	AN-R<AN-BP=AN-Cross
Substance abuse	Present	8.8%	26.3%	35.2%	<0.001	AN-R<AN-BP=AN-Cross
Family alcohol abuse/dependence	Present	19.4%	29.9%	34.7%	0.04	AN-R<AN-BP=AN-Cross
TCI-R novelty seeking score	Mean (SD)	95.57 (15.13)	99.35 (15.12)	108.47 (15.40)	<0.001	AN-Cross>AN-BP=AN-R

Note: AN-R =Anorexia Nervosa Restrictive Subtype; AN-BP = Anorexia Nervosa Purging-Bingeing Subtype; AN-Cross = Anorexia Nervosa patients who crossed over to Bulimia Nervosa.

8.3. Study 3

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LIFETIME COMORBIDITY OF TOBACCO, ALCOHOL AND DRUG USE IN EATING DISORDERS: A EUROPEAN MULTICENTER STUDY

During the last two decades, a body of research has indicated that substance use problems are common among women with eating disorders (EDs) (e.g. Bulik et al., 2004; Fernandez-Aranda et al., 2008; Karwautz et al., 2002). In 1994 a review conducted by Holderness and collaborators evaluated 51 studies and revealed that up to 10% of women with the restricting subtype of AN and 41% with BN suffered from co-occurring substance use disorders (Holderness et al., 1994). The interpretation of the literature on the comorbidity between EDs is however complicated by methodological shortcomings, such as a failure to control for confounding variables, the heterogeneity of the populations (ages, diagnostic criteria, disorder subtypes, severity) and the variety of technologies used to evaluate substance. The present study was part of the Fifth European Framework project on Healthy Eating and adds to the existing literature by extending previous findings and including several methodological improvements.

OBJECTIVES

1.) To assess the differences in comorbid lifetime substance use (tobacco, alcohol and drug use) between eating disorder (ED) patients and healthy controls in five different European countries.

3.) To evaluate whether there were differences in substance use among the distinct ED sub diagnosis.

2.) To assess whether there were differences across countries in the prevalence of substance use.

Figure 1: Map of Europe

METHOD

A total of 1664 participants took part in the present study. ED cases (n= 879) were referred for assessment and treatment to specialized ED units in five different European countries (Spain, Austria, Italia, Slovenia and the UK) diagnosed according to DSM-IV criteria. Healthy controls (n=785) with similar demographic features to the clinical participants were ascertained from various community sources from the same catchment area.

ASSESSMENT

Participants completed the Substance Use Subscale of the Cross-Cultural (Environmental) Questionnaire (CCQ), a retrospective measure, which has been developed as part of a European Multicenter trial in order to detect dimensions associated with EDs in different countries. In the control group, also the GHQ-28, the SCID-I interview and the EAT-26 were used.

Table 1: Comparison of prevalence for lifetime substance use: ED patients vs controls

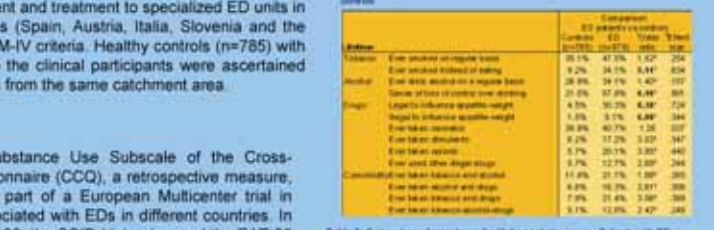


Table 2: Comparison of prevalence for lifetime substance use: Patients with EDs: comparison for diagnose subtype

RESULTS

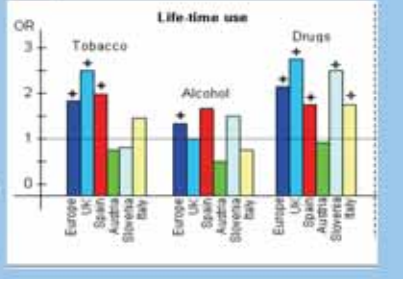
- ED patients had higher lifetime and current tobacco and general drug use.
- The only non-significant result was obtained for lifetime and current alcohol use.
- Significant differences across ED subdiagnoses and controls also emerged, with BN and AN-BP generally presenting the highest and AN-R and controls the lowest rates.
- The only exception was detected for alcohol use where EDNOS demonstrated the highest values.
- Only a few cultural differences between countries emerged.

Table 3: Comparison of prevalence for lifetime substance use: Patients with EDs' comparison for prevalence

CONCLUSIONS

- With the exception of alcohol consumption, tobacco and drug use appear to be more prevalent in ED patients than healthy controls.
- The differential risk observed in patients with bulimic features might be related to differences in temperament or might be the result of increased sensitivity to reward.
- Longitudinal designs which examine the potentional mediating role of dysregulated eating as a risk factor for substance use will be of interest.

Figure 2: Comparison for ED patients vs control (OR adjusted by age, sex, and education)



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DRUG and ALCOHOL DEPENDENCE

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Present and lifetime comorbidity of tobacco, alcohol and drug use in eating disorders: A European multicenter study

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Abstract

Objectives: To assess the differences in comorbid lifetime and current substance use (tobacco, alcohol and drug use) between eating disorder (ED) patients and healthy controls in five different European countries.
Method: A total of 1664 participants took part in the present study. ED cases ($n = 879$) were referred to specialized ED units in five European countries. The ED cases were compared to a balanced control group of 785 healthy individuals.
Assessment: Participants completed the Substance Use Subscale of the Cross Cultural (Environmental) Questionnaire (CCQ), a measure of lifetime tobacco, alcohol and drug use. In the control group, also the GHQ-28, the SCID-I interview and the EAT-26 were used.
Results: ED patients had higher lifetime and current tobacco and general drug use. The only non-significant result was obtained for lifetime and current alcohol use. Significant differences across ED subdiagnoses and controls also emerged, with BN and AN-BP generally presenting the highest and AN-R and controls the lowest rates. The only exception was detected for alcohol use where EDNOS demonstrated the highest values. Only a few cultural differences between countries emerged.
Conclusions: With the exception of alcohol consumption, tobacco and drug use appear to be more prevalent in ED patients than healthy controls. The differential risk observed in patients with bulimic features might be related to differences in temperament or might be the result of increased sensitivity to reward.

Keywords: Eating disorders; Tobacco use; Alcohol use; Drug use; Cultural differences

1. Introduction

During the last two decades, a body of research has indicated that substance use problems are common among women with eating disorders (EDs) (e.g. (Bulik et al., 2004; Fernandez-Aranda et al., 2008; Karwautz et al., 2001, 2002;

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Thompson-Brenner et al., 2008). In 1994 a review conducted by Holderness and collaborators evaluated 51 studies and revealed that up to 10% of women with the restricting subtype of AN and 41% with BN suffered from co-occurring substance use disorders (Holderness et al., 1994). The prevalence of substance use in eating disordered individuals has however been found to vary considerably across studies, which could be attributable to the fact that researchers have commonly treated substances as one homogenous group. Only more recently have investigations looked at a variety of licit and illicit substances separately (Anzengruber et al., 2006; Bulik et al., 2004; Gadalla and Piran, 2007a; Piran and Gadalla, 2007). The present study adds to the existing literature by assessing tobacco, alcohol and drug use in a large case–control sample across various ED subtypes in several European countries.

1.1. Tobacco and eating disorders

In relation to tobacco use prevalence estimates for ED patients have been found to vary between 58.1% and 68.1% (Anzengruber et al., 2006). Given the well-known effects of smoking on weight and appetite, it is not surprising that this behaviour is often utilized as a weight control method in patients with EDs (Austin and Gortmaker, 2001; Croll et al., 2002; Delnevo et al., 2003; George and Waller, 2005). Accordingly, various studies have indicated that smoking behaviour has been found to be more widespread in individuals with EDs than in controls (Corte and Stein, 2000; John et al., 2006; Saules et al., 2004; Welch and Fairburn, 1998) and that AN individuals with bulimic symptomatology exhibited the highest rates (Haug and Guarda, 2001; Wiederman and Pryor, 1996a,b).

1.2. Alcohol and eating disorders

The prevalence estimate of alcohol use disorder (AUD) in ED patients has been reported to be as high as 30–50% (Dansky et al., 2000). A recent meta-analysis (Gadalla and Piran, 2007a) on the co-occurrence of EDs and alcohol use disorders including 41 studies found that the magnitude of the associations between ED patterns and AUD ranged from small to medium size and was statistically significant for any ED. The strongest relationship with alcohol use was found for bulimic BN individuals, followed by patients suffering from binge eating disorder (BED) and eating disorder not otherwise specified (EDNOS). However, no association was found between AN and AUD. In total, only 4 out of the 41 studies reported a negative relationship between disturbed eating behaviour and AUD.

1.3. Drug use and eating disorders

Finally, as regards to drug use, prevalence rates in treatment seeking ED patients have been indicated to vary between 7.9% and 32.6% (Corcos et al., 2001). A recent meta-analysis of 16 studies on the association between drug use and EDs found a higher prevalence of drug abuse for BN, the prevalence was lower for BED and people with AN had lower levels of drug abuse than healthy populations (Calero et al., submitted for publication).

Most studies assessing drug use in ED patients have failed to specify the nature of the drug, whether it is a street drug (cocaine, heroin, stimulants) or a prescribed medication (tranquilizers, hypnotics, antidepressants). Differentiating the distinct classes of drugs is nevertheless imperative, since some drugs such as for instance cocaine and amphetamines are known to act as appetite suppressants and are therefore employed for the purpose of weight loss, while others such as cannabis have appetite-stimulating properties (Gadalla and Piran, 2007b; Nappo et al., 2002; Saules et al., 2004). The small number of studies that examined these distinct types of drugs separately demonstrated a positive relationship between dieting and bingeing (with or without purging) and stimulants, amphetamines, cocaine and psychotropic medications (Corcos et al., 2001; McCabe and Boyd, 2005; Piran and Robinson, 2006).

1.4. Cultural differences in substance use and EDs

Research on cultural differences in the comorbidity of substance use in ED patients has predominantly assessed ethnic groups living in Anglo Saxon societies (French et al., 1997; Granner et al., 2001). Only more recently have studies from Japan (Nagata et al., 2002), Mexico (Gutierrez et al., 2001) and some European countries (Beato-Fernández et al., 2007; García-Vilches et al., 2002) emerged. However, no study has undertaken a cross-cultural comparison study of substance use in EDs across various countries/regions. This omission in the literature leaves unanswered questions concerning how environmental factors among different cultures could influence the comorbidity of EDs and substance use. This study therefore reports on the prevalence of substance use in EDs across various ED subtypes in several European countries using a common instrument.

Taken together, there is evidence that tobacco, alcohol and drug use commonly co-occur with EDs and that this association is somewhat stronger with bulimic behaviours, than in individuals who are purely restrictive. Nevertheless, it should be acknowledged that little previous research has addressed this topic, and that the few findings that have been reported have been conflicting. Furthermore preceding research is complicated by methodological shortcomings, such as a failure to control for confounding variables, the heterogeneity of the populations (ages, diagnostic criteria, disorder subtypes, severity) and the variety of technologies used to evaluate substance abuse.

1.5. Aims of the study

The present study was part of the Fifth European Framework project on Healthy Eating, which is a collaboration of eight countries with the common task to examine the individual and environmental factors related to EDs. The overall aim of this study was to replicate and extend previous findings and include several methodological improvements. Primarily, we employed a large sample size of ED patients and healthy controls from various different European countries. Secondly, the present study included participants across the range of EDs including EDNOS

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patients. Virtually nothing is known about EDNOS and substance use even though clinically it is the most common sort of ED (Dalle Grave and Caluqi, 2007; Machado et al., 2007). The few studies assessing substance use in EDNOS patients have indicated a high rate of comorbidity also in these patients (Le Grange et al., 2006; Striegel-Moore et al., 1999). This exclusion is critical since the severity of psychopathology and degree of secondary psychosocial impairment in those with EDNOS has been found to be comparable to those seen in patients with AN or BN (Krug et al., 2008a; Ricca et al., 2001; Turner and Bryant-Waugh, 2004). Finally, we assessed a broad range of licit and illicit substances with differing physiological properties.

Our primary hypothesis is that people with binge eating will have a higher rate of substance abuse. A secondary hypothesis is that substances with appetite suppressant properties might be consumed more frequently than substances not containing these characteristics. A third hypothesis was that environmental differences such as the substance availability across cultures would be reflected in the prevalence of the ED population.

2. Method

2.1. Participants

The present study employed a case–control design. Six centers from five different European countries (two for Italy) participated in the current study: the University Hospital of Bellvitge, Barcelona, Spain (262-eating disorder (ED); 160-C (Controls); the Department of Child and Adolescent Psychiatry, Medical University of Vienna (94-ED; 59-C); the Eating Disorders Research Unit, Institute of Psychiatry, London, UK (319-ED; 184-C); the Department of Neurology and Psychiatric Services, University of Florence, Italy (50-ED; 50-C); the Department of Psychiatry, Fondazione Centro del Monte Tabor, Milan, Italy (93-ED; 101-C) and the University Psychiatric Hospital, University of Ljubljana, Slovenia (61-ED; 231-C).

Entry into the study was between March 2001 and September 2002. The total sample comprised 1664 participants ($n = 1555$ females; $n = 109$ males), 879 ED patients (22.1% with AN-restrictive (AN-R), 20.0% with AN–binge–purging (AN-BP), 32.1% with BN and 25.8% with EDNOS) and 785 healthy controls. The mean age was 25.8 years (S.D. = 8.7). Due to the limited sample size of BN non-purging individuals a distinction between purging and non-purging BN subtypes could not be made.

Most of the *ED participants* were ascertained from clinical institutions and were ill at assessment. A small proportion (less than 20%) came from community sources e.g. user or carer organizations or from advertisements. Participants were diagnosed according to DSM-IV-R (APA, 2000a) criteria, using a semi-structured clinical interview [SCID-I (First et al., 1996)] or EATATE [only used in Austria and the UK (Anderluh et al., 2008)], carried out by experienced psychologists and psychiatrists. The interviewers were trained in the administration of these instruments although formal inter-rater reliability was not computed for this study.

The exclusion criteria for the present study were: (a) missing values for any diagnostic items DSM-IV-TR criteria (APA, 2000a) for AN, BN, or for EDNOS); (b) younger than 16 years old; (c) unable to complete the assessment because of cognitive impairment, mental retardation and/or serious medical condition; or, (d) current psychotic disorder. For the present analysis, the following individuals had to be excluded from an initial sample of 901 patients: (a) patients ($N = 18$) with missing values for any diagnostic tools; (b) cognitive impairment ($N = 2$); (c) comorbid psychotic disorder ($N = 2$). Diagnostic decisions were made by psychologists or psychiatrists who completed the anamnesis together with the treatment team according to published treatment guidelines (APA, 2000b).

Healthy controls were ascertained from various community sources at each site and were asked to volunteer in a study of factors associated with the development of EDs. All controls were from the same catchment areas as index patients. The final control group included 785 volunteers. The exclusion criteria for the control group were: (a) younger than 16 years; (b) a lifetime history of health or mental illnesses (including EDs), screened by the General Health Questionnaire-28 (Goldberg, 1981) the SCID I (First et al., 1996) according to DSM-IV-R criteria (APA, 2000a) and the EAT-26 [total score > 20 (APA, 1994; Garner et al., 1982)]. From the initial sample of 791 controls, 6 participants were excluded, who had had a lifetime ED. Each site obtained ethical approval separately from its own institutional review board.

2.2. Assessment

2.2.1. The substance use subscale of the cross-cultural (environmental) questionnaire. This retrospective self-administered questionnaire has 51 items with 6 subscales. It was developed by an expert group from various European countries in order to detect environmental factors associated with the development of EDs. The CCQ was based on the major instruments in the field of EDs, which are the Oxford Risk Factor Interview (Fairburn et al., 1997, 1998) and the McKnight Risk Factor Interview (Shisslak et al., 1999). It was developed by an expert group from various European countries in order to detect environmental factors associated with the development of EDs. A more detailed description of the CCQ can be found in an earlier publication (Fernandez-Aranda et al., 2007). A recent study (Penelo et al., submitted for publication) on the psychometric properties of the CCQ offers preliminary evidence that it is a useful and valid screening instrument to assess past and present risk factors of EDs in a variety of different countries.

In the current study, only the 13 items of the substance use domain were used. These assess both lifetime and current substance use. Licit substances include alcohol and tobacco (current tobacco use was defined as number of cigarettes smoked per day). Psychoactive substances were broken down into four discrete groups, including (1) cannabis (dope, hash or marijuana), (2) stimulants (cocaine, crack, amphetamines or speed); (3) opioids/heroin and tranquillizers (valium, Librium, mogadon or) and (4) other illegal drugs (LSD, magic mushrooms, ketamine, ecstasy, glue/aerosols). Other questions asked about the age that drug consumption began, number of cigarettes smoked per day and amount of alcohol consumed during a typical week (number of units ranged from 1 unit = 1 single (25 ml) measure of spirits e.g. whisky, gin or vodka to 28 units = 1 bottle (700 ml) of spirits), sense of loss of control over drinking and whether the person smoked cigarettes, or took legal or illegal drugs and/or medicine to influence appetite or weight. A copy of the whole instrument can be requested from the corresponding author.

2.2.2. EATATE phenotype interview. The EATATE interview was developed for the European Healthy Eating Project. It is a semi-structured interview, comprising a European adaptation of the longitudinal interval follow-up evaluation [LIFE, (Keller et al., 1987)] and the eating disorders examination [EDE, (Fairburn and Cooper, 1993)]. The interview is used to obtain a lifetime history of ED symptoms, which are then plotted on a lifeline. The EATATE instrument has been used previously in AN research (Anderluh et al., 2008) and demonstrates good inter-rater reliability in terms of diagnoses (kappa 0.82–1.0) and illness history variables (0.80–0.99).

2.2.3. General health questionnaire-28 (GHQ-28). The GHQ-28 is a self-report questionnaire that has been designed to detect and assess individuals with an increased probability of a present psychiatric disorder. The GHQ-28 has been studied in various European countries and has been found to be a valid and reliable tool (Goldberg, 1981).

2.2.4. Eating attitudes test (EAT-26). The EAT-26, which is an abbreviated version of the EAT-40 questionnaire (Garner and Garfinkel, 1979), assesses a broad range of symptoms and provides a total score for disturbed eating attitudes and behaviour. This instrument has acceptable criterion-related validity with Cronbach's alphas ranging from 0.82 to 0.89 in a previous study (Garner et al., 1982).

2.3. Procedure

Participants were invited to participate in a collaborative, multicenter study across Europe, investigating associated ED factors. All patients were first

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assessed by board certified psychologists or psychiatrists using a two hour structured diagnostic face-to-face or phone interview to measure ED symptoms and psychopathological traits. Eating disorder diagnoses were based on this interview and were consensually derived among members of the clinical team who had participated in the assessment. An information sheet at the start of the questionnaire informed the participants about the purpose of the study and assured confidentiality of the results. Furthermore, it was emphasized that participation in the study was completely voluntary and that participants were free to withdraw from the study at any time.

2.4. Statistical analyses

The statistical analysis was carried out with the SPSS 15.0.1 program for Windows. First, prevalence rates of tobacco, alcohol and drug use were estimated, for the total European sample and for each country. Next, odds ratios for substance use comparing ED patients with controls were calculated through logistic regression models adjusted by sex, age and education. The adjusted OR value assessed the extent of the association between the presence of the disorder (independent variable) and the utilization of tobacco, alcohol and drugs (dependent variables): a significant OR higher than 1 indicates that the ED patients reported a higher probability of using substances than controls. Clinical significance was also estimated by the calculation of the effect size for proportions based on Cohen's *d* index (Cohen, 1988). Results were interpreted as small if *d* values were lower than 0.2, medium for *d* values ranging between 0.2 and 0.5 and large for *d* values higher than 0.5.

Second, the prevalence of substance use was compared across ED groups and also across geographical origins (country). The independent variables comprised the ED subtype (AN-R/AN-BP/BN/EDNOS) and the geographical origin (UK/Spain/Austria/Slovenia/Italy). Outcomes were the use of each substance. Statistical comparisons were based on logistic regressions adjusted by sex, age and education.

Finally, adjusted odds ratios (by sex, age and education) also compared the substance use between each ED subtype and the control group. A significant OR value higher than 1 indicates that the ED patients (diagnosed with a concrete ED subtype) had a higher risk of using substances than healthy controls.

Since multiple statistical testing was carried out, type-I error inflation was controlled through Bonferroni–Holm's adjustment (Holm, 1979).

3. Results

3.1. Socio-demographic description of the participants

Table 1 contains the socio-demographic characteristics for the total sample stratified by country. Age differed significantly between the two groups, with the eating disordered patients being older than the controls. The two groups also differed slightly in sex, with the ED group comprising significantly more females than the control group. There were no differences in the distribution of sex across ED subtypes ($\chi^2 = 0.83$; $p = 0.84$). Furthermore more ED patients were employed and had grown up in urban places. Conversely, significantly more controls than ED patients were currently studying. The age of starting smoking and drinking did not differ between groups. The closeness of the population matching varied between countries. In the Slovenian sample in particular the ED patients were significantly older than the controls.

3.2. Comparison of substance use across gender

No statistically significant differences across sex were found for the prevalence estimates of substances use, except for lifetime (males 11.2% vs. females 22.8, $p = 0.007$) and current

Table 1
Socio-demographic characteristics by country: percentages for categorical variables and mean (S.D.) for quantitative variables

	Total European		United Kingdom		Spain		Austria		Slovenia		Italy	
	ED ($n = 879$) AN-R = 172 AN-BP = 156 BN = 250 EDNOS = 201	Controls ($n = 785$)	ED ($n = 319$) AN-R = 68 AN-BP = 75 BN = 48 EDNOS = 128	Controls ($n = 184$)	ED ($n = 262$) AN-R = 40 AN-BP = 40 BN = 113 EDNOS = 48	Controls ($n = 160$)	ED ($n = 94$) AN-R = 22 AN-BP = 8 BN = 32 EDNOS = 17	Controls ($n = 59$)	ED ($n = 61$)[b]	Controls ($n = 231$)	ED ($n = 143$) AN-R = 42 AN-BP = 33 BN = 57 EDNOS = 8	Controls ($n = 151$)
Age: mean (S.D.)	27.2 (8.9)[a]	24.3 (8.2)[a]	29.1 (11.4)	26.8 (11.5)	25.3 (5.6)	26.1 (5.5)	27.1 (8.3)	24.2 (6.3)	25.7 (7.0)[a]	18.7 (4.4)[a]	27.2 (7.7)	25.6 (6.1)
Gender: female (%)	96.6[a]	91.2[a]	97.2	98.9	93.9[a]	85.5[a]	100	96.6	98.2[a]	83.0[a]	97.2	98.0
Education level:												
Primary (%)	8.2[a]	24.8[a]	0[a]	0[a]	15.4[a]	3.8[a]	0	1.7	9.1[a]	74.5[a]	12.6[a]	9.9[a]
Secondary (%)	50.1[a]	25.6[a]	47.6[a]	31.9[a]	43.6[a]	11.3[a]	0	3.4	58.2[a]	21.6[a]	65.7[a]	47.7[a]
University (%)	41.8[a]	49.6[a]	52.4[a]	68.1[a]	40.9[a]	84.9[a]	100	94.9	32.7[a]	3.9[a]	21.7[a]	42.4[a]
Employment status: employed (%)	54.9[a]	39.1[a]	51.9	60.7	62.5[a]	45.8[a]	64.7	61.0	51.4[a]	5.7[a]	44.7	55.0
Students (%)	47.8[a]	75.3[a]	54.2	60.7	41.6[a]	75.6[a]	53.8[a]	98.3[a]	60.7[a]	94.3[a]	37.9[a]	55.0[a]
Area where brought up: urban (%)	69.0[a]	56.8[a]	70.2	68.9	73.8	77.8	80	55.9	38.2	31.6	69.0	58.9
Age started smoking: mean (S.D.)	17.1 (3.2)	16.6 (2.8)	16.4 (3.3)	16.8 (3.3)	16.9 (2.6)	17.4 (2.4)	17.8 (3.8)	16.4 (2.7)	17.6 (2.7)[a]	15.2 (1.8)[a]	18.3 (3.4)	17.8 (3.0)
Age started drinking alcohol: mean (S.D.)	18.6 (4.4)	18.1 (2.9)	18.6 (4.7)	18.1 (2.5)	17.8 (3.5)	18.7 (2.9)	19.1 (4.6)	17.2 (2.9)	18.1 (2.8)	16.2 (2.9)	19.0 (3.6)	20.1 (3.4)

[a] Significant comparison (with Bonferroni–Holm's correction) based on chi-square tests for categorical variables and *t*-test for quantitative variable. S.D.: standard deviation.
[b] Data from Slovenia is not included due the lack of diagnose subtype in this country.

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(7.1% vs. 19.0%; $p = 0.003$) smoking instead of eating, currently smoking more than 10 cigarettes/day (8.9% vs. 17.6%, $p = 0.046$), lifetime sense of loss of control over drinking (26.3% vs. 41.4%, $p = 0.003$) and lifetime intake of legal drugs to influence appetite and weight (10.2% vs. 18.4%, $p = 0.041$). Comparisons stratified by diagnosis status (separate analyses for ED and control participants) showed no statistical differences by sex for substance use in the ED patients cohort. However, considering only control participants, compared to men, women reported currently higher percentage of sense of loss of control over drinking (22.9% vs. 8.7%, $p = 0.006$), higher prevalence of daily smoking (at least 10 cigarettes/day; 10.8% vs. 1.7%, $p = 0.028$), higher proportion of smoking instead of eating (9.9% vs. 1.5%, $p = 0.021$) and lower proportion of cannabis (37.7% vs. 50.0%, $p = 0.047$) and other drugs use (5.1% vs. 11.6%, $p = 0.027$).

3.3. Lifetime and current comorbidity for substance use: OR values

Regarding the association between substance use in the total European sample, comorbidities (OR coefficients adjusted by sex, age and education) showed a clear positive lifetime and current co-occurrence between tobacco and drugs and between alcohol and drugs, in both ED and control cohorts. These coefficients were also significant when stratified by ED subtype. OR values for alcohol and drugs ranged between 2.9 (control cohort) and 6.1 (AN-BP subtype), and between 1.7 (EDNOS subtype) and 8.0 (AN-R subtype) for tobacco and drugs. While lifetime tobacco and lifetime alcohol use were also related, no significant relationship were revealed for current use of these substances. Results stratified by country were quite similar, with only a few exceptions located in the control cohorts: (a) lifetime tobacco and lifetime alcohol consumption were not associated in Spain (OR = 1.70, $p = 0.356$) and Italy (OR = 2.07, $p = 0.092$); (b) current alcohol and current drug use were not statistically correlated in Spain (OR = 2.33, $p = 0.141$), Austria (OR = 1.90, $p = 0.467$) and Slovenia (OR = 2.54, $p = 0.103$); and finally (c) current tobacco and current alcohol use were related in Spain (OR = 5.65, $p = 0.010$) and Austria (OR = 5.39, $p = 0.012$).

3.4. Comparison of substance use between ED patients and controls

Fig. 1 summarizes the global comparison of tobacco, alcohol and drug use between ED patients and controls, adjusted by age, sex and education, for the whole sample and by countries. The presence of an ED (disorder) was positively associate with the use of tobacco in the total European sample (lifetime use: OR = 1.74; current use: OR = 1.72), in the UK (lifetime use: OR = 2.57; current use: OR = 2.25), in Spain (lifetime: OR = 2.00; current use: OR = 1.77) and Italy (current use: OR = 1.85). Similarly a positive relationship between total drug use was revealed for the total European sample (lifetime use: OR = 2.25; current use: OR = 2.30), the UK (lifetime use: OR = 2.74; current use: OR = 2.05), Spain (lifetime use: OR = 1.61), Slovenia (lifetime use: OR = 2.55) and Italy (lifetime use: OR = 1.72). However, the occurrence of current alcohol use was lower for ED patients than controls in the UK (OR = 0.52) and Italy (OR = 0.33).

Table 2 shows the detailed comparison of lifetime and current substance use for controls and ED patients. For the total European sample, lifetime prevalence estimates were significantly higher for ED patients than healthy controls for tobacco (47.5% vs. 35.1%, $p < 0.0005$), alcohol (34.1% vs. 26.9%, $p = 0.002$) and drug (61.3% vs. 43.3%, $p < 0.0005$) use. As regards to current use, estimates were higher for ED patients than controls for tobacco (34.8% vs. 24.2%, $p < 0.0005$) and drug (34.4% vs. 22.1%, $p < 0.0005$) use but not for alcohol (24.6% for ED vs. 26.1% for healthy subjects, $p = 0.481$) consumption. OR coefficients that measure the degree of association between substances use and the presence of the disorders showed that compared to controls, ED patients reported a higher prevalence estimate for all substances, except for alcohol and cannabis use. Furthermore, compared to controls, ED patients endorsed the reason for substance use as an appetite suppressant significantly more often: smoking instead of eating (OR = 5.11) and taking legal drugs (OR = 8.38) or illegal drugs (OR = 6.00) to influence appetite–weight.

Similar patterns were observed for current tobacco, alcohol and drug use. Number of cigarettes smoked per day was higher

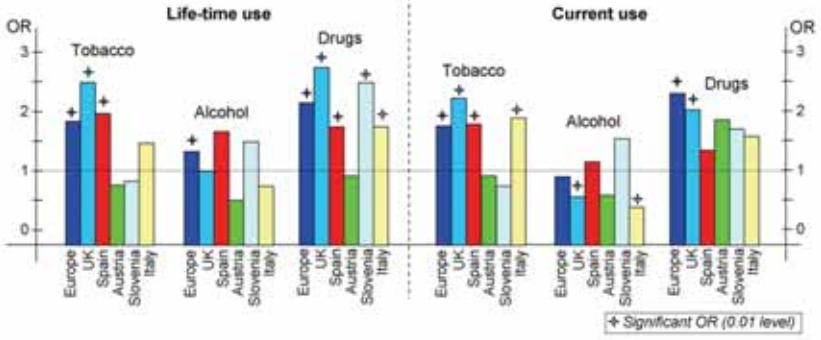

Fig. 1. Comparison for ED patients vs. control (OR adjusted by age, sex and education).

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Table 2
Comparison of prevalence for lifetime and current substances use

	Comparison ED patients vs. controls				Patients with ED: comparison for diagnose subtype					Patients with ED: comparison for prevalence					
	Controls (n = 785) (%)	EDs (n = 879) (%)	Odds ratio[a]	Effect size[b]	AN-R (n = 172) (%)	AN-BP (n = 156) (%)	BN (n = 250) (%)	EDNOS (n = 201) (%)	p	UK (n = 339) (%)	Spain (n = 262) (%)	Austria (n = 94) (%)	Slovenia (n = 61) (%)	Italy (n = 143) (%)	p
Lifetime															
Tobacco															
Ever smoked on regular basis	35.1	47.5	1.52*	0.254	35.5	55.3	57.4	44.3	0.003	39.9	56.3	52.2	32.7	49.3	<0.0005
Ever smoked instead of eating	9.2	34.1	**5.11***	0.634	17.5	43.6	45.3	31.5	<0.0005	32.5	43.1	36.0	21.4	24.8	<0.0005
Alcohol															
Ever drink alcohol on a regular basis	26.9	34.1	1.40*	0.157	31.3	43.2	29.5	**43.7**	0.010	62.8	15.1	34.4	16.3	17.0	<0.0005
Sense of loss of control over drinking	21.5	37.9	**6.10***	0.801	42.9	64.6	77.1	53.5	<0.0005	43.9	87.1	29.7	10.3	63.6	<0.0005
Drugs															
Legal to influence appetite–weight	4.5	30.3	**8.38***	0.724	10.8	34.4	43.3	28.6	<0.0005	32.9	29.8	29.3	23.6	29.1	0.617
Illegal to influence appetite–weight	1.5	9.1	**6.00***	0.344	3.0	10.5	15.1	7.6	0.022	10.6	8.3	9.8	7.3	7.9	0.565
Ever taken cannabis	38.9	40.7	1.28	0.037	27.5	40.5	**49.8**	42.6	<0.0005	44.8	43.9	36.3	40.0	29.8	0.075
Ever taken stimulants	6.2	17.2	3.01*	0.347	5.6	24.7	27.2	17.2	<0.0005	19.4	20.6	12.1	9.1	12.8	0.070
Ever taken opioids	5.7	20.1	3.85*	0.440	10.8	31.0	27.7	14.0	<0.0005	24.0	22.2	13.2	3.6	19.1	0.062
Ever used other illegal drugs	5.7	12.7	2.68*	0.244	6.1	22.2	13.4	12.3	0.001	10.6	9.4	7.8	10.9	8.5	0.801
Comorbidity															
Ever taken tobacco and alcohol	11.4	21.1	1.88*	0.265	15.5	26.2	22.4	25.4	0.312	32.2	12.0	29.2	10.9	14.3	<0.0005
Ever taken alcohol and drugs	6.6	16.3	2.61*	0.308	8.1	27.0	19.8	14.6	0.001	28.7	7.7	13.6	9.1	10.8	<0.0005
Ever taken tobacco and drugs	7.9	21.4	3.06*	0.389	10.6	29.8	29.6	17.9	<0.0005	22.0	25.6	16.9	11.1	20.0	0.148
Ever taken tobacco-alcohol-drugs	5.1	12.0	2.43*	0.249	5.7	18.4	15.4	11.2	0.070	16.4	6.9	12.6	7.4	9.4	0.089
Current															
Tobacco															
Currently smoke cigarettes	24.2	34.8	1.56*	0.234	22.9	47.0	46.7	24.9	<0.0005	21.6	46.3	44.0	19.6	40.8	<0.0005
Number of cigarettes/day >10	9.9	23.9	2.68*	0.360	21.5	23.6	32.1	21.9	0.160	21.3	29.8	27.0	12.2	34.5	0.110
Currently smoke instead of eating	9.1	26.8	3.66*	0.474	11.0	36.9	39.4	21.1	<0.0005	21.0	36.5	28.2	11.5	26.1	<0.0005
Alcohol															
Currently drink alcohol	26.1	24.6	0.92	0.034	20.7	29.3	19.7	**38.3**	<0.0005	46.1	9.5	23.9	7.1	10.6	<0.0005
Amount of alcohol: >21 units/week	3.0	3.9	1.41	0.049	1.2	8.0	3.8	6.7	0.132	9.4	0.4	2.2	0.0	1.4	0.007
Sense of loss of control over drinking	10.5	24.4	**3.04***	0.373	17.7	31.8	29.2	25.6	0.011	34.5	22.0	20.0	3.6	17.7	<0.0005
Drugs															
Currently take cannabis	20.0	23.6	**1.64***	0.097	17.1	23.6	**29.8**	24.5	0.050	29.6	25.5	8.9	18.2	21.3	0.153
Currently take stimulants	1.0	7.8	9.29*	0.356	0.0	12.1	11.8	8.5	0.809	9.9	10.2	2.2	1.8	6.4	0.240
Currently take opioids	2.3	13.6	6.54*	0.427	7.0	22.1	16.4	10.3	0.014	16.6	10.6	6.6	1.8	13.5	0.160
Currently take other illegal drugs	2.0	3.7	2.58	0.102	1.4	9.1	5.8	3.7	0.268	6.0	3.3	1.1	0.0	4.3	0.350
Comorbidity															
Currently take tobacco and alcohol	6.7	9.1	1.22	0.089	4.8	12.8	11.3	8.9	0.034	11.1	4.3	15.6	3.6	7.8	0.286
Currently take alcohol and drugs	1.7	6.9	3.99*	0.258	1.4	12.6	7.0	11.7	0.008	13.7	5.6	4.5	0.0	4.3	0.016
Currently take tobacco and drugs	2.0	10.2	5.74*	0.348	3.6	16.2	13.9	7.9	0.017	8.0	13.4	6.9	1.9	12.9	0.166
Currently take tobacco, alcohol and drugs	0.9	4.3	5.18*	0.215	0.7	8.2	5.1	5.6	0.076	4.8	4.7	4.6	0.0	4.3	0.994

ED: eating disorder; AN-R: anorexia nervosa restrictive subtype; AN-BP: anorexia nervosa bulimic and/or purging subtype; BN: bulimia nervosa; EDNOS: eating disorder not otherwise specified. UK: United Kingdom. Comparison based logistic regression models adjusted by sex, age and education. * $p < 0.01$ – most relevant values are represented in bold and are stated in the text.

[a] Significant adjusted OR (with Bonferroni–Holm's correction).

[b] Coefficient based on Cohen's *d*.

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in the ED group compared to the control group (OR = 2.68). However, no significant differences were observed between both groups for current alcohol use and amount of alcohol drunk per week. Yet loss of control over drinking was higher in ED patients than controls for both lifetime (OR = 6.10) and current (OR = 3.04) measures. Finally, current cannabis use was higher in ED patients than controls (OR = 1.64).

3.5. Comparison of substance use across diagnostic subtypes of ED

Within the ED patients, BN and AN-BP patients had the highest prevalence for most lifetime and current tobacco, drug use and comorbid substance use variables whereas AN-R participants generally displayed the lowest, followed by EDNOS patients. However, as regards to lifetime and current alcohol consumption EDNOS patients exhibited the highest prevalence estimates (lifetime use: $p = 0.010$; current use: $p < 0.0005$). Interestingly for both lifetime and current alcohol use AN-R individuals also revealed higher values than BN but not AN-BP patients. Finally for lifetime and current cannabis use, the EDNOS sample also reported higher values than the AN-BP but not BN group (lifetime use: $p < 0.0005$; current use: $p = 0.050$).

Similar findings can be found in Table 3, where the first column contains p-values for the comparison of controls vs. AN-R, AN-BP, BN and EDNOS. This is the significance level obtained selecting controls as reference group in the logistic models. Most comparisons are significant. The other columns contain the ORs which have been obtained for the comparison of each diagnostic subtype and controls. Generally, compared to controls, BN and AN-BP patients display a significantly higher risk for consuming tobacco, drugs and co-occurring substance use but not alcohol consumption. For lifetime alcohol use only AN-BP and EDNOS patients report higher risk than the controls, but for current use the results are statistically equal for all types of EDs. Finally, AN-R patients generally have an equal risk than controls to abuse all kind of substances.

3.6. Comparison of substance use in ED patients coming from different countries

Table 2 shows that the highest levels of tobacco use were found in Spain and Austria, and the lowest in Slovenia. Regular drinking was more frequent ($p < 0.0005$) in the UK, followed by Austria. Regarding comorbidities, alcohol was specially associated with tobacco ($p = 0.034$) and drugs ($p = 0.008$), with the highest co-occurrences in UK and Spain. In relation to current use, the patterns of prevalence were quite similar, excepting the use of more than 10 cigarettes/day and the comorbidities, with no differences across countries (the only exception was the simultaneous use of alcohol and drugs, with higher prevalences for UK, $p = 0.016$). Finally, the comparison of ED samples from different countries for lifetime substance use showed no statistical differences in drugs, except for other illegal drugs ($p = 0.001$).

4. Discussion

We were able to partially confirm our initial hypothesis in that we found that the prevalence of smoking, and drug use as well as the majority of the co-concurrent substance use variables were higher in the ED patients than the control group. Conversely, overall there was no higher level of alcohol consumption. Our second hypothesis, that ED patients would consume significantly more substances with appetite suppressant properties was only partially confirmed. While we revealed that tobacco use was higher in the ED group, stimulants were not used significantly more commonly than opioids and cannabis. Our third hypothesis was also only partially confirmed since we found that BN and AN-BP patients consumed tobacco and drugs more commonly than the remaining ED subgroups. However, alcohol was most frequently employed by EDNOS and AN-BP patients. Finally, our fourth hypothesis that cross-cultural difference would emerge was confirmed only to some extent, since only a few differences across countries were detected.

4.1. Substance use in eating disordered individuals and healthy controls

4.1.1. Tobacco use and eating disorders. Our first aim was to assess whether ED individuals and controls differed in the consumption of tobacco, alcohol and drugs. In accordance with previous studies (Anzengruber et al., 2006; Saules et al., 2004; Welch and Fairburn, 1998; Wiseman et al., 1998) the present findings indicated that the presence of an ED was positively associated with the use of both lifetime and current tobacco use in the total European sample. Moreover, we also revealed that ED individuals employed smoking significantly more often as a weight control method than healthy controls. Similarly, various studies have indicated that women concerned about their body weight were more likely to start smoking than those with fewer weight concerns and less dissatisfaction with body shape (Croll et al., 2002).

4.1.2. Alcohol use and eating disorders. We found no differences between ED patients and controls in lifetime and current alcohol consumption and the amount of alcohol drunk per week. This contrast previous reviews which have generally found a positive association between alcohol use and EDs (Gadalla and Piran, 2007b; Holderness et al., 1994). Low statistical power could to some extent explain these discrepant findings or it is possible that European samples differ from North American samples in this respect. However, although eating disordered patients were not regular heavy drinkers they reported more frequently a sense of loss of control over drinking (the effect size for this variable was high).

4.1.3. Drug use and eating disorders. With regards to drug use we found that the odds of lifetime and current drug use were higher for the ED patients than the healthy controls. These results agree with previous reviews (Calero et al., submitted for publication; Holderness et al., 1994). However, when different

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Table 3
Comparison of the prevalence for lifetime and current substances use between each diagnosis subtype and controls: OR adjusted by age, sex and education

	p	AN-R	AN-BP	BN	EDNOS
Lifetime					
Tobacco					
Ever smoked on regular basis	<0.0005	1.05	2.13[a]	2.11[a]	1.28
Ever smoked instead of eating	<0.0005	2.01[a]	7.96[a]	8.47[a]	4.17[a]
Alcohol					
Ever drink alcohol on a regular basis	<0.0005	1.29	2.03[a]	1.11	2.07[a]
Sense of loss of control over drinking	<0.0005	3.47[a]	7.56[a]	18.4[a]	4.85[a]
Drugs					
Legal to influence appetite–weight	<0.0005	2.49[a]	10.30[a]	14.80[a]	7.54[a]
Illegal to influence appetite–weight	<0.0005	2.28	7.35[a]	9.73[a]	5.26[a]
Ever taken cannabis	<0.0005	0.70	1.26	1.94[a]	1.31
Ever taken stimulants	<0.0005	0.63	4.98[a]	4.70[a]	2.79[a]
Ever taken opioids	<0.0005	2.07	6.75[a]	5.76[a]	2.24[a]
Ever used other illegal drugs	<0.0005	1.31	5.47[a]	2.93[a]	2.35[a]
Comorbidity					
Ever taken tobacco and alcohol	<0.0005	1.43	2.47[a]	2.04[a]	2.24[a]
Ever taken alcohol and drugs	<0.0005	1.40	4.93[a]	3.33[a]	1.93[a]
Ever taken tobacco and drugs	<0.0005	1.45	4.80[a]	4.77[a]	2.04[a]
Ever taken tobacco-alcohol-drugs	<0.0005	1.30	4.08[a]	3.23[a]	1.87
Current					
Tobacco					
Currently smoke cigarettes	<0.0005	0.93	2.79[a]	2.32[a]	0.98
Number of cigarettes/day: >10	<0.0005	2.16[a]	2.73[a]	4.13[a]	2.49[a]
Currently smoke instead of eating	<0.0005	1.10	6.29[a]	6.72[a]	2.60[a]
Alcohol					
Currently drink alcohol	0.014	0.72	1.21	0.69	1.69
Amount of alcohol: >21 units/week	0.630	0.46	2.21	1.25	2.42
Sense of loss of control over drinking	<0.0005	1.95[a]	4.78[a]	4.09[a]	2.99[a]
Drugs					
Currently take cannabis	<0.0005	1.13	1.64	2.40[a]	1.66
Currently take stimulants	<0.0005	0.01	16.0[a]	14.1[a]	10.5[a]
Currently take opioids	<0.0005	3.66[a]	11.3[a]	7.60[a]	4.99[a]
Currently take other Illegal drugs	0.018	0.94	3.41	4.00[a]	2.14
Comorbidity					
Currently take tobacco and alcohol	0.280	0.49	2.09	1.59	1.09
Currently take alcohol and drugs	<0.0005	0.93	7.96[a]	3.54[a]	7.30[a]
Currently take tobacco and drugs	<0.0005	2.22	10.1[a]	7.47[a]	4.59[a]
Currently take tobacco, alcohol and drugs	<0.0005	1.03	11.6[a]	5.35[a]	7.02[a]

AN-R: anorexia nervosa restrictive subtype; AN-BP: anorexia nervosa bulimic and/or purging subtype; BN: bulimia nervosa; EDNOS: eating disorder not otherwise specified. Comparison based on logistic regressions adjusted by sex, age and education. The column with *p*-values corresponds to the global comparison between ED subtypes and control cohort.

[a] Significant adjusted OR (with Bonferroni–Holm's correction).

types of drugs and lifetime and current drug use were assessed individually, no statistically significant differences were found for lifetime cannabis use and current use of illegal drugs. Moderately weak effects may to some extent explain these incoherent findings.

In contrast to our expectations, drugs containing appetite suppressant properties were not consumed more frequently than the other types. However, in accordance with our predictions eating disturbed individuals stated that they employed legal or illegal drugs to influence weight and appetite, significantly more often than controls (Nappo et al., 2002).

4.1.4. Comorbidity of tobacco, alcohol and drugs in eating disorders. The finding of substance use comorbidity was similar to that found in previous reports (Blinder et al., 2006; Ross and Ivis, 1999; Wiederman and Pryor, 1996b). In accordance with our findings, researchers have suggested that individuals who consume more than one substance may have specific personality vulnerability factors (Alvarez-Moya et al., 2007; Baker et al., 2007; Davis and Claridge, 1998; Holderness et al., 1994). Although in a previous study (Alvarez-Moya et al., submitted for publication), common personality traits (namely higher novelty seeking and both lower self-directedness and reward dependence) were observed in patients with EDs and comorbid substance abuse, empirical evidence about the existence of an "addictive personality" is as yet inconclusive (Conason et al., 2006; Holderness et al., 1994).

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4.2. Comparison of substance use between subtypes of ED

The findings from this study confirm previous studies in revealing that BN and AN-BP patients had the highest risk of smoking (Haug and Guarda, 2001; Wiederman and Pryor, 1996b) and drug use (Blinder et al., 2006; Calero et al., submitted for publication; Fernandez-Aranda et al., 2008). The result of lifetime and current alcohol consumption that was higher in EDNOS than in BN individuals also fits with findings in the literature (Corte and Stein, 2000; Grilo et al., 1995a,b; Schmidt et al., 2006).

The increased risk of substance abuse in people with bulimic symptomatology might be related to differences in temperament such as higher levels of disinhibition or impulsivity in this group (Fernandez-Aranda et al., 2006; Fernandez-Aranda et al., 2008; Thompson-Brenner et al., 2008). Another possibility is that this is an acquired change in reward sensitivity (O'Brien and Treasure, submitted for publication; Treasure, 2007; Piran and Gadalla, 2007; Gadalla and Piran, 2007b). Understanding the link between addictions and bulimic symptomatology, especially binge eating has also been increased by the development of animal models. Animals "binge eat" if they are exposed to some of the environmental factors (food restriction, street, intermittent exposure to highly palatable food etc.) thought to play a role in the development of human EDs (Avena et al., 2005; Corwin, 2006; Corwin and Hajnal, 2005; Corwin and Buda-Levin, 2004; Lewis et al., 2005; Rada et al., 2005). Research has indicated that not only do these animals over eat palatable food but they have also been shown to be more prone to develop addictive behaviours when exposed to alcohol and cocaine (Koob and Le Moal, 2005; Robinson and Berridge, 2003).

4.3. Substance use in eating disorders across countries

The fourth aim of the present study was to examine whether there were differences across countries in tobacco, alcohol and drug use. Some differences across countries emerged. Both lifetime and current tobacco use was found to be higher in patients from the UK and Spain. A similar trend was found for lifetime drug use. This parallels the findings from a current report on drug consumption in European populations which reported that Spain and the UK had the highest substance use prevalence rates (European Monitoring Centre for Drugs and Drug Addiction, 2007). These findings suggest that it is the relative accessibility of drugs as evidenced by population levels that determines the level of usage in ED patients.

4.4. Limitations

The results of this study must be interpreted within the context of some methodological limitations. Firstly, the retrospective, self-report data collection procedures and the case mix including a high proportion of clinical cases may have limited the validity and the reliability of our findings. Secondly, as the study was correlational, we cannot draw firm conclusions about the direction of the relationships between the problem behaviours and the dispositional variables. Thirdly, we did not have sufficient information to accurately time the age of onset of the ED, and so we were unable to examine the temporal aspects of drug use in relation to this. Fourthly, we were not able to differentiate between alcohol use, abuse and dependence. Fifthly, it was not possible to quantify the common comorbidities associated with EDs i.e. depression, anxiety, obsessive compulsive disorder. Finally, the sample sizes (for ED subtypes and control cohorts) and the success of the matching between controls and patients varied between the different countries, which could have affected the accuracy of the p-values and the estimations in the regression models. Notwithstanding these limitations, we were able to assess the nature of the comorbid relationship between EDs and substance use in a large and phenotypically well-characterized sample of individuals with EDs across five European countries.

4.5. Treatment implications

These results emphasize the importance of assessing substance use in individuals with disturbed eating behaviour, and vice versa. As regards to treatment it may be that treatment focused on both eating and addictive behaviours together may be warranted (Benjamin and Wulfert, 2005; Sinha and O'Malley, 2000). Preferably such treatment ought to focus on characteristics of both disorders, which could be accomplished by employing psychoeducation, the assessment of high risk situations and relapse prevention techniques (Benjamin and Wulfert, 2005; Ricciardelli and McCabe, 2001; Sinha and O'Malley, 2000). Finally, clinicians should also try to modulate unconstructive emotional conditions or impulsive stress and/or anxiety release, which could be achieved by incorporating affect-oriented elements (e.g. dialectical behaviour therapy) with the goal of improving the adaptive management of these emotions (Krug et al., 2008b; McMain et al., 2001).

4.6. Conclusion

This is the first study examining the relationship between EDs and lifetime and current tobacco, alcohol and drug use of a wide range of drug classes and ED diagnoses across different European countries. The association between substance use and binge eating disorders in particular has been confirmed. Longitudinal designs which examine the potential mediating role of dysregulated eating as a risk factor for substance use will be of interest.

Conflict of interest

All other authors declare that they have no conflicts of interest.

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Contributors: All authors designed the study, wrote the protocol and managed the literature searches and summaries of previous related work. Roser Granero and Eva Penelo undertook the statistical analysis, and Isabel Krug, Janet Treasure and Fernando Fernandez-Aranda wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

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8.4. Study

CONTEXTUAL CONDITIONING OF EATING RESPONSE AND THE ROLE OF ENERGY DENSITY OF FOOD IN RATS.

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INTRODUCTION

Eating disorders (EDs) characterised by bingeing behaviour generally comprise bulimia nervosa (BN); binge/purge-type of anorexia nervosa (AN) and binge eating disorders (BED) (APA, 1994). Even though substantial research on these disorders has been carried out, knowledge about the etiopathological factors associated with binge eating continues to be elusive. (Grilo, Masheb, & Wilson, 2001) Jansen (1998) has developed an account for binge eating based on pavlovian conditioning. This model states that a systematic association of a variety of cues with food intake can cause an over ingestion. These cues will eventually become a good predictor of food consumption and as a result will acquire the capacity to evoke adaptive physiological reactions for digestion such as insulin release in blood and salivary flow (Nederkoorn & Jansen, 2002).This phenomenon, known as cue reactivity, is generally experienced by the individual as appetite or craving and most probably leads to an increased food ingestion.

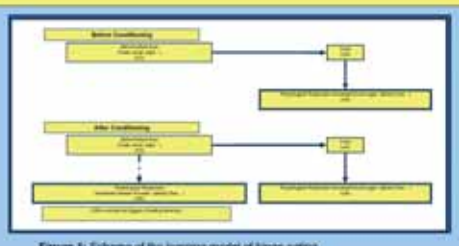


Figure 1: Schema of the learning model of binge eating

OBJECTIVES

The main aims of this research was to investigate (1) whether a specific context could elicit eating in rats as a result of conditioning and (2) whether conditioning depended on the density of food.

METHOD

Participants: the subjects were 32, 90 day old, naive female hooded Long-Evan rats, with a mean ad lib weight of 240 g.

Apparatus: Two sets of cages, both distinctively different from the home cages and located in different rooms, served as the experimental contexts. In addition to the standard laboratory chow food (high-density food), an especially prepared pap-diet (low-density food) was administered to the animals via a drinking bottle.

Procedure: Thirty two restricted rats experienced two contexts. They had access to food in context A, but no food was available in context B. Half of the animals received high dense energy food (HD groups) whereas the other half received low dense energy food (LD groups) during conditioning sessions. Half of the animals in each type of food group were tested in context A and the other half in context B.

Table 2 summarizes the design of the Experiment

Table 1: Design of the Experiment

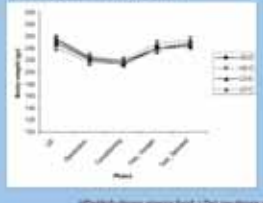
Groups	Restriction (7 days)	Conditioning (10 days)		Reloading (8 days)	Test1 (2 hours restricted) (1 day	Test2 (Ballast) (1 day)
HD – C	Yes	Ctxt A -> Chow	Ctxt B -> no food	Pap in Home cages	Chow in Ctxt A	Chow in Ctxt A
HD – NC		Ctxt A -> no food	Ctxt B -> Chow			
LD - C		Ctxt A -> Pap	Ctxt B -> no food	Chow in Home cages	Pap in Ctxt A	Pap in Ctxt A
LD – NC		Ctxt A -> no food	Ctxt B -> Pap			

HD-C: High-Density Food-Conditioned; HD-NC:High-Density Food-Non-Conditioned; LD-C:Low-Density Food-Conditioned; LD-NC:Low-Density Food Non-Conditioned

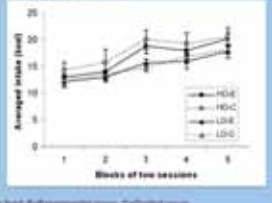
RESULTS

- The rats' body weight fell throughout the deprivation and conditioning phases but it was recuperated on the second test session.
- All groups increased the number of kcal ingested throughout the conditioning phase. However, HD-groups consumed more than the LD groups
- As can be seen from Figure 1 the HD-E group ate more than the other three groups and the HD-C group ate less than the other groups in both test sessions (after 3 hours of food restriction a and after no restriction, respectively).

Graph 1: Groups mean body weight during the different phases of the experiment



Graph 2: Groups mean intake in Kcal throughout the conditioning phase



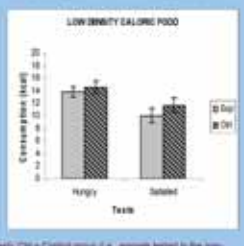
HD=High-dense energy food; LD=Low-dense energy food; E=Experimental group; C=Control group

CONCLUSIONS

The results of this experiment provide support for contextual conditioning of food intake in rats. In addition we found that this conditioning only took place with food, which was high in density. Applying these results to humans, the present findings suggest that a variety of cues could after a systematic association with food intake, provoke the over binge eating behaviour in individuals suffering from EDs. These findings also have clinical value in the sense that the ultimate way to extinguish these responses, is cue exposure with response prevention.

Figure 1: Groups mean intake in kcal for hungry condition (left-hand) and satiated condition (right-hand) during test. For high density caloric food

Figure 2: Groups mean intake in kcal for hungry condition (left-hand) and satiated condition (right-hand) during test. For low density caloric food



Exp = Experimental group (i.e., animals tested in the conditioned context); Ctrl = Control group (i.e., animals tested in the non-conditioned context).

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Title:

IS CONTEXTUAL-POTENTIATED EATING DEPENDENT ON CALORIC DENSITY OF FOOD?

(¿ES LA POTENCIACIÓN CONTEXTUAL DE LA CONDUCTA DE COMER DEPENDIENTE DE LA DENSIDAD CALÓRICA DEL ALIMENTO?)

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Short title:

CONDITIONED EATING RESPONSE

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Abstract

One experiment tested whether a specific context could elicit eating in rats as a result of Pavlovian conditioning and whether this effect depended on the caloric density of food. Thirty two deprived rats experienced two contexts. They had access to food in context A, but no food was available in context B. During conditioning, half of the animals received high density caloric food (HD groups) whereas the other half, low density caloric food (LD groups). Then, half of the rats in each type of food group was tested in context A and the other half in context B. The results demonstrated an effect of context conditioning only in HD groups. These findings suggest the relevance of both contextual conditioning and caloric density of food in eating behaviour. Implications for the aetiology of binge eating will be discussed.

Keywords: cue reactivity, caloric density, binge eating, potentiated eating, Pavlovian conditioning, rats.

Resumen

Se puso a prueba en un experimento con ratas si un contexto específico podría provocar la conducta de comer como resultado del condicionamiento Pavloviano, y si este efecto dependía de la densidad calórica del alimento. Treinta y dos ratas privadas de comida experimentaron dos contextos. Los animales tenían acceso al alimento en el contexto A, pero nunca encontraron alimento en el contexto B. La mitad de los animales recibió un alimento de alta densidad calórica (grupos HD) mientras que la otra mitad recibió un alimento de baja densidad calórica (grupos LD) durante las sesiones de condicionamiento. Posteriormente, la mitad de los animales en cada tipo de alimento se puso a prueba en el contexto A y la otra mitad en el contexto B. Los resultados mostraron un efecto de condicionamiento contextual solamente en los grupos HD. Estos resultados sugieren la importancia del condicionamiento del contexto y de la densidad calórica del alimento en la conducta de comer. Se discuten las implicaciones que estos hallazgos pueden tener en la etiología de la conducta de atracón.

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INTRODUCTION

Eating is controlled by both physiological mechanisms and a number of learned cues (Woods, 2005). Weingarten (1983) found that an auditory stimulus (CS) presented systematically paired with 8 ml. of milk (US) elicited feeding on test days even though rats were tested while satiated. Working with Preschool children, Birch, McPhee, Sullivan, and Johnson (1989) found that when the children were in a room previously associated with food and eating, they initiated a meal quicker, and had a larger meal, than when they were in a different room that had never been related to food and eating. During testing the children were satiated. In a recent and related experiment, with rats, Petrovich, Ross, Gallagher, and Holland (2007) have reported that a contextual conditioned stimulus (CS), which was paired with consumption of food pellets, enhanced consumption in animals that were not food-deprived on test. Moreover, these authors found that this cue-potentiated eating, as they call this enhanced eating, was observed only when the food presented during the test was the same as that used in the training phase. These authors have suggested that the mechanism that mediates cue-enhanced eating does not involve induction of general motivation to eat, but rather the selective enhancement of consumption of the food US.

The aim of the present study is to replicate the contextual cue-potentiated eating effect and to extend its analysis to the role that caloric density of food could play in this conditioning.

Flavour-nutrient associations have been extensively studied (see Capaldi, 1996, for a review). For instance, Ramirez (1994) reported that rats given access to a saccharin solution paired with intra-gastric (IG) carbohydrate infusions drank 70% more saccharin than did rats given the saccharin solution paired with IG water. On the other hand, evidence for learned preferences based on nutrient concentration is provided by studies in which rats were trained to consume, on alternate days, a flavoured nutritive source and a differently flavoured and less concentrated source. On subsequent choice tests with the two flavours presented in otherwise identical sources, rats usually preferred the flavour previously paired with the higher nutrient

concentration (e.g., Ackroff, and Sclafani, 2006; Arbour, and Wilkie, 1988; Bolles, Hayward, and Crandall, 1981; Hayward, 1983; Warwick, Synowski, Coons, and Hendrickson, 1999, but see Van Vort, and Smith, 1983; Sclafani, Nissenbaum, and Ackroff, 1994; Lucas, Azzara and Sclafani, 1998, for the opposite results).

In the studies cited above the rats were given fixed amounts of fluids, each one with a different concentration of nutrients. With this procedure the rats are given different concentrations and different amounts of nutrients. Any resulting flavour preference could be explained by the number of calories paired with each flavour as well as the differential density of fluids. Nevertheless, Bolles, *et al.* (1981) showed that caloric density was more important than the number of calories in developing a preference for a given flavour. Preference was greater for a flavour associated with 2 g of a 4-calorie food than for a flavour associated with 4 g of a 2-calorie food.

In addition to flavours, context can also be associated with postingestive effects of food. Agmo, and Marroquin, (1997) found that a sweet and nutritive solution was more effective in producing a place preference than a plain sweet solution. However, as far as we know, no study has assessed whether caloric density plays a role in cue-potentiated eating.

In the experiment reported here, one group of rats always had access to high density food (HD-diet) in a specific context A, while they did not have access to food in a second context B. An additional group had the same experience except that they received a low density food (LD-diet) instead of the HD-diet. Following conditioning, fifty per cent of the rats in each diet condition was tested in the conditioned context A (groups HD-Paired and LD-Paired), and the other fifty percent in the non-conditioned context B (groups HD-Unpaired and LD-Unpaired). Contextual conditioning will be evident if animals eat more in the conditioned context than in the non-conditioned context. Furthermore, if the context paired with HD-diet is able to develop a stronger association with this type of food in comparison with a second context paired with LD-diet, then the former context must elicit a more vigorous CR (greater intake) than the latter context during testing.

METHOD

Subjects: The subjects were thirty-two naïve female hooded Long Evans rats reared in the Animal Laboratory at the University of Barcelona. At the start of the experiment they were approximately 90 days old and weighing between 223 and 270 g. They were housed in pairs in home cages made of semitransparent white plastic, 50x25x15 cm. The colony room had a

temperature and humidity-controlled environment, and a 12:12 light/dark cycle. Throughout the experiment, water was freely available, but food was restricted as detailed below. The University of Barcelona Animal Care and Use Committee approved all procedures.

Apparatus: Two sets of cages, both distinctively different from the home cages and located in different rooms, served as the experimental contexts. The walls and floors of all these cages were made of plastic and the roofs of wire mesh (i.e., with room for both solid food as well as bottles -when they were available). The first set of cages was placed in a room highly illuminated by two fluorescent lamps. These cages measured 40x25x18 cm; their walls and floors were transparent. The floor was covered with commercial cat litter with lavender essence. This context will be referred to as "light context" hereafter. The second set of cages were smaller, in a room which was maintained in semidarkness, illuminated only by a single infra-red ray bulb located in a corner far away from the cages. The floors of the cages were covered with wood shavings. This second context will be referred to as "dark context" hereafter. Animals in this phase (and also during testing) were run individually.

The HD-diet was commercial laboratory rodent chow diet (maintenance A-04, Panlab, S.A.; nutritive quality: 15.4% protein, 2.9% fat, 60.5% carbohydrate, 12% moisture, and 9.2% fibres and minerals; 3.17 kcal/g). The LD-diet was an especially prepared diet consisting of 200 ml semi-skimmed milk; 200 ml water; 50 g baby food and 15 g powder milk (nutritive quality: 3.2% protein, 0.8% fat, 13,1% carbohydrate, 82.5% moisture, and 0.4% fibres and minerals; 0.72 kcal/g). The LD-diet was designed so that it maintained the same proportions of nutrients as the HD-diet (commercial laboratory rodent chow diet), but with a lower caloric-density. The LD-diet was administered to the animals via a drinking bottle, which was placed on the wire mesh roof.

Procedure: During the whole experiment rats were weighed every day at 8:00 am. The body weight of the animals was controlled in order to prevent a weight fall below 80% of their initial body weight. During the experimental sessions, the rats were always run individually.

Baseline Phase: During the first four days, before starting the deprivation schedule, a weight baseline was established.

Deprivation Phase: Over the next seven days, rats received a food deprivation schedule in their home cages. Food was taken away at about 5:00 p.m. on the last day of the baseline phase and then was administered at 8:30 am every day. On the first day, animals had access to food for 6 hours. On the following days, this duration was gradually lowered, so that on the last day of deprivation, access to food was limited to 1 hour only. On the last three days of the

deprivation phase, all rats were introduced to the new LD-diet in order to reduce any novelty effects of this kind of food. Thus, during the feeding period, animals had access to both, HD- and LD- diets. At the end of this deprivation phase, rats were assigned to each group in such a way that the LD-diet consumption in the LD- groups (Paired and Unpaired) equated the HD-diet consumption in the HD- groups (Paired and Unpaired). In order to make consumptions of both kinds of food comparable, intake was measured in kcal. Also animals were weight matched into LD- groups and HD- groups (n=8 in each group: HD-Paired, HD-Unpaired, LD-Paired, and LD-Unpaired). By the last day of this restriction phase the animals' body weight ranged from 195 to 241 g.

Conditioning phase: Following the deprivation phase, all rats began the conditioning phase, which lasted 10 consecutive days. Animals received 2 daily sessions, each of them 1 hour long. The first daily session always took place at 9:00 am and the second daily session was carried out at 15:00 pm. Contexts (Light vs. Dark) were counter-balanced across groups. That is, during the first session half of the animals in each group were placed in the Light context and the other half in the Dark context. During the first daily session food was administered to all animals. Rats in the HD-groups had access to the HD-diet, and animals in the LD-groups had access to the LD-diet. Consumption was recorded by weighing the food, any diet, to the nearest tenth of a gram on an electronic scale before and after the 1-hour eating period. The difference indicated the amount of food the rats had consumed during each session. During the second daily session, animals were placed in the alternative contexts, but this time no food was presented to them. The rats had free access to water during the two daily sessions. After each session rats were immediately transported back to their home cages, where they remained until the next session. Since by day 5 of the conditioning phase the body weight of some rats had fallen below 80% of their baseline weight, all animals had access to a 30 min period of supplementary food at 19:00 pm in their home cages and until the end of the conditioning phase. For HD-groups, the supplementary food was LD-diet while for the LD-groups, HD-diet. The alternative diets were used as maintenance food in order to keep the contingency between each context and the experimental diet. On the last day of this phase the body weight of groups LD ranged from 189 to 234 g., whereas that of groups HD varied from 198 to 237 g.

Test Phase: After the conditioning phase the test phase lasted for six days. This phase had two test days which were intermixed with four refeeding days. Test days were conducted on days 3 and 6 of this phase, while refeeding days on days 1, 2, 4, and 5. On refeeding days all rats had "ad libitum" access to the supplementary food (i.e., animals in groups HD received LD-diet, and rats in groups LD received HD-diet) in the home-cages. On test days animals had access to the conditioned diet (i.e., animals in groups HD received HD-diet, and rats in groups LD received LD-diet). One group of each diet was tested in the conditioned context (i.e., groups HD-Paired and LD-Paired), while the remaining groups were tested in the non-conditioned context (i.e., groups HD-Unpaired and LD-Unpaired). The body weight ranges

for each group, averaging the two test days, were: 224-247 g; 215-263 g; 229-255 g; and 222-255 g, respectively. On the first test session, food was removed three hours before testing (Hungry test); while on the second test session, food was maintained until testing (Satiated test). Each test session started at 12:00 noon and lasted for one hour.

Statistical Analyses: Prior to any analysis, all data from the two test sessions were explored with a box-and-whisker plot (Tukey, 1977) in order to identify any outlier values. Then, multivariate analyses of variance (MANOVA) were carried out, followed by simple effects analysis if an interaction was significant. Throughout this article, a significance level of $p < 0.05$ was adopted for all statistical analyses.

RESULTS

Three animals were excluded from the analysis because a box-and-whisker plot identified their food consumption as outlier values during testing. One animal of the LD-Unpaired group ate 1.47 kcal while the consumption of the rest of the animals in this group ranged between 10.99 and 18.89 kcal. Another rat of the HD-Unpaired group ate 35.58 kcal while the rest of the animals ranged between 5.27 and 18.33 kcal. The third rat, of group HD-Paired, ate 3.78 kcal while the rest of animals in this group ranged between 13.24 and 24.08 kcal. Finally, all groups had 7 animals except group LD-Paired, which had 8.

The consumption of each diet throughout the last three days of the deprivation phase was similar. Although the proportion of HD-diet intake for all animals was 0.51, there were some individual differences. Therefore, rats were assigned to each diet condition according to their preferences. The proportion of HD-diet intake during the baseline phase in groups which had access to this diet during conditioning was 0.59 and the proportion of LD-diet intake in groups which had access to LD-diet during conditioning was 0.58. An ANOVA confirmed that the consumption of the selected experimental diet did not differ between groups (Highest F=0.06).

The rats' body weight fell throughout the deprivation and conditioning phases but it was recuperated on the second test session. A MANOVA with diet (HD-diet vs. LD-diet) and conditioning (Paired vs. Unpaired contexts) as between factors and sessions as a within factor was conducted. For the analysis of the rats´ weight, the weight of the last session of phases baseline, deprivation and conditioning was considered; as well as the weights of the two test sessions. This analysis revealed a significant main effect of sessions, $F(4,100)=385.3$, $p<0.001$; and the conditioning x sessions interaction was also significant, $F(4,100)=3.3$,

p=0.015. No other factor or interaction was significant (highest F=2.6). In order to analyse the interaction conditioning x sessions, univariate ANOVAs were conducted session by session. The factor of conditioning did not differ in any session (all Fs<1). On the other hand, all sessions differed among each other at both levels of conditioning factor (Bonferroni contrasts, p<0.05), except the comparison between baseline and the second test session in the Unpaired groups.

All groups increased the number of kcal ingested throughout the conditioning phase. However, HD- groups consumed more than LD- groups. A MANOVA with diet (HD-diet vs. LD-diet), conditioning (Paired vs. Unpaired contexts) and context (Light vs. Dark) as between factors and sessions as a within factor confirmed these observations. This analysis revealed that the main factors diet, context and sessions were significant, F(1,21)=6.3, p=0.020, F(1,21)=5.3, p=0.032 and F(9,189)=17.8, p<0.001, respectively. The interactions diet x context and sessions x diet x context were also significant, F(1,21)=5.1, p=0.035 and F(9,189)=2.0, p=0.040, respectively. No other factor or interaction was significant (highest F=2.0). In order to analyse the interaction diet x context, univariate ANOVAs were conducted at each level of both factors. The factor context at HD-diet and the factor diet at light context were significant, F(1,12)=5.4, p=0.038 and F(1,12)=12.1, p=0.004, respectively. In particular, rats ate more kcals when the diet was HD-diet and they had access to it in the light context. No other comparison was significant (all Fs<1). Univariate ANOVAs were also conducted session by session in order to analyze the significant third interaction diet x context x sessions. While on sessions 1 and 6 the interaction diet x context was significant, F(1,25)=10.6, p=0.003 and F(1,25)=7.0, p=0.014, respectively; it was very close to significance on sessions 3 and 4, F(1,25)=4.2, p=0.051 and F(1,25)=4.1, p=0.053, respectively. On the remaining sessions the interaction diet x context was not significant (highest F=2.0). Besides, the main factor context was significant on sessions 2 and 6, F(1,25)=6.2, p=0.020 and F(1,25)=8.1, p=0.009, respectively; as well as diet on sessions 5 and 6, F(1,25)=12.5, p=0.002 and F(1,25)=9.5, p=0.005, respectively. None of the two factors was significant in the remaining sessions (highest F=3,3), although context was very close to significance on session 8, F(1,25)=4.1, p=0.053.

Figure 1 shows the food intake (shown in kcal) during the two test sessions of the four groups (i.e., left-hand side: HD-Paired and HD-Unpaired groups; right-hand side: LD-Paired and LD-Unpaired groups). The HD-Paired group ate more than the other three groups and the HD-Unpaired group ate less than the other groups in both test sessions (after 3 hours of food restriction and after no restriction, respectively). A MANOVA with diet, (HD-diet vs. LD-diet), conditioning (Paired vs. Unpaired contexts) and context (Light vs. Dark) as between factors and test as a within factor, showed that the main factors conditioning and test were significant, F(1,21)=4.4, p=0.049, and F(1,21) =10.8, p=0.003, respectively; as well as the interaction diet x conditioning, F(1,21)=8.4, p=0.009. But neither the main factors diet and context, nor the remaining interactions were statistically significant (highest Fs=3.3). Further

analysis of the interaction diet x conditioning revealed that the factor conditioning differed in the HD-diet, $F(1,12)= 8.9$ (p=0.012), but did not differ in the LD-diet, $F<1$. On the other hand, the two diets differed in the Paired groups, $F(1,13)= 6.6$ (p=0,024), but did not differ in the Unpaired groups, $F(1,12)= 4.1$ (p=0.065).

(Figure 1 about here)

GENERAL DISCUSSION

The present study had two main aims: firstly, to replicate the findings reported by Petrovich *et al*. (2007) in which contextual cues related to food intake elicited higher consumption than an alternative context which had never been paired with food; secondly, to examine whether the caloric density of food had an effect on the cue-potentiated eating.

The present results clearly show that contextual cues can serve as conditioned cues to stimulate eating when HD-diet was used as a US but, surprisingly, they fail to show such an effect when LD-diet was presented as a US. In fact, the results observed in the HD- groups replicate those reported by Petrovich *et al.* (2007). In a related study, Weingarten (1983) found that a tone paired with milk potentiated eating. Similarly, working with children, cue-potentiated eating mediated by context has also been reported by Birch, McPhee, Sullivan, and Johnson (1989).

The null result observed in LD- groups could be interpreted in several ways. Firstly, it is reasonable to assume that HD-diet is more effective as a US than LD-diet. Supporting this argument, a large number of studies have reported that a flavoured-cue paired with nutrient can allow a flavour-nutrient association, and that this association depends on the caloric density of food (e.g., Ackroff, and Sclafani, 2006; Arbour, and Wilkie, 1988; Azzara and Sclafani, 1998; Warwick, *et al*., 1999). However, it is worth mentioning that in all these experiments nutritive density of food covaried with the net amount of consumed nutrients. Such a fact allows an alternative explanation because the observed flavour preferences could be explained both by the density of the food as well as by the absolute number of calories consumed. Although in the current experiment the rats of HD- groups ingested more kcal than the rats in LD- groups during the conditioning phase, these differences disappeared throughout the last four sessions of conditioning, where groups HD- and LD- differed in terms of food-density rather than ingested kcal. In this sense, our results seem to agree with those reported by Bolles *et al*. (1981) who gave rats 2 g of a 4-calorie food or 4 g of a 2-calorie food. In this way, they ensured that the amount of nutrients was identical in both

conditions, HD and LD, although the two conditions differed in density. Their results showed a greater preference for a flavour paired with more dense food.

Another possibility in order to explain the differences observed between diets is based on anticipatory negative contrast (Flaherty and Checke, 1982). The effectiveness of a reinforcer is reduced if it is closely accompanied by a second preferred reinforcer (see, Mackintosh, 1974). Flaherty and Checke (1982) showed that consumption of saccharine was reduced if saccharine was followed by more preferred sucrose. Note that, in the experiment reported here, animals in the LD- groups received HD-diet in the evening, and thus they could learn to anticipate a more reinforcing food when they were moved to the experimental contexts. However, the 2.5-hours delay from the end of the last experimental session until the beginning of access to HD-diet in their home-cages could be long enough to prevent any association between the last experimental session and HD-diet and, therefore, the anticipatory contrast effect. In fact, Flaherty and Checke (1982) found that delayed sucrose delivery reduced saccharine consumption only when it was delivered within 30 min.

A third possibility is based on Treit and Spetch's (1986) proposal that rat's caloric intake is controlled by two factors: under certain conditions control is by caloric learning, and under other conditions by a caloric metering mechanism. The metering mechanism refers to the ability of rats to precisely calculate the caloric density of foods. Thus, it could be argued that the rats of groups, HD- and LD-, had metered the density of HD-diet and LD-diet, and therefore that, throughout the conditioning phase, they could have learned to adjust their consumptions in order to obtain the needed nutrients of both types of food. Effectively, rats in the LD- groups ate a large amount of LD-diet; enough to provide them with a very similar quantity of nutrients as those consumed by HD- rats during the conditioning phase. This was confirmed in a thorough inspection of the daily consumption during the last four days of this phase, which showed that HD- rats ate an average of 6.15 g., while LD- animals ate an average of 23.82 g.; and this distribution provided approximately the same amount of kcal for each source of food. It is also reasonable to argue that some characteristics of LD-diet, like its smell, taste, etc., could have been associated with the low density diet and, as a consequence, they could have activated a greater consumption regardless of the context where that kind of food was found. Therefore, it is possible that on the test sessions the ingestion size might be controlled by different cues: by some food features in the presence of LD-diet, and by contextual cues with HD-diet. If this line of reasoning is correct, differences could be expected to be found between the Paired and Unpaired groups on tests with HD-diet, and that these differences will disappear with LD-diet.

Another interesting detail from the interaction between diets and conditioning (see Figure 1) is the fact that both Paired groups differed between each other, and that the difference between the unpaired groups was close to significance. It is important to realize that the

procedure used in this experiment is similar to the "differential rocedure", which is used to study inhibitory conditioning. In this procedure, one stimulus (a CS+) is paired with the US, and a second stimulus (a CS-) is presented alone (i.e., is followed by the absence of the US). Often inhibitory conditioning is behaviourally silent and therefore additional tests are necessary to measure it, like summation and retardation tests. In the summation or compound stimulus test (Rescorla, 1969; Pavlov, 1927), the effects of a supposedly inhibitory stimulus (CS-) presented in compound with an excitatory stimulus (CS+) are observed. In the retardation of the acquisition test (Rescorla, 1969), a supposedly inhibitory stimulus (CS-) is expected to cause a retardation when learning an excitatory conditioning in comparison with a neutral stimulus. For example, Maes and Vossen (1995) found a differential inhibition effect using contextual stimuli. In their experiment rats received an electric footshock during training, which was consistently delivered in one context, but not in a second context. Subsequent summation and retardation tests showed that the second context had acquired inhibitory properties. Having in mind this procedure, it is possible that whereas the paired context acted as an excitatory CS+ eliciting eating, the unpaired context (i.e., the context that systematically signalled the absence of food) could have acquired inhibitory properties and could thus have acted as an inhibitory CS–, which in turn could have reduced the food ingestion. Accordingly, in the present study, this interpretation could account for differences in the food consumption between the unpaired groups. The explicit unpaired presentations of the non-conditioned context and the food could have allowed the animals to learn a negative relation between the cues and could therefore have produced an inhibitory conditioning effect. Unfortunately, there is not an appropriate control condition to state that the unpaired context acquired inhibitory properties. Further research is certainly needed to address all these questions.

Implications for bingeing behaviour.

The fact that a context-nutrient association can potentiate eating behaviour has important implications. It means that this kind of association does not only affect food selection via enhancing a flavour or a context preference, but also that it can produce overeating. Furthermore, if context-nutrient association was selective for HD-diet then any learning model of binge eating, must consider this fact.

Although we are conscious of the limitations of this study, the results of the present experiment could suggest the existence of interesting variables which could take part in the aetiology of binge eating.

The term bingeing behaviour refers to the consumption of a large amount of food in a discrete period of time during which loss of control is experienced (APA, 1994). Even though up to

this date substantial research has been carried out on this behaviour, knowledge of its aetiology remains unclear (Crowther, Sanftner, Bonifazi & Shepherd, 2001; Grilo, Masheb & Wilson, 2001; Vanderlinden, Dalle Grave, Fernandez, Vandereycken, Pieters & Noorduin, 2004). One of the models proposed to account for bingeing behaviour is Jansen's (1998) theory of cue reactivity based on classical conditioning.

Jansen's (1998) cue reactivity theory states that after systematic associations of cues (the conditioned stimulus, CS) with food (the unconditioned stimulus, US), the CS cues will reliably signal food. When these cues are good predictors of food, they acquire the ability to elicit adaptive physiological responses for digestion,, such as salivation and insulin release. These classical conditioned responses (CRs) are supposed to be experienced as appetite, or even craving, and therefore increase the likelihood of food intake. The predictive cues are often directly related to food (such as the smell, the sight and the taste of food), but they might also be contextual cues (e.g., being at home, being alone) or interoceptive cues (e.g., specific feelings or cognitions) (Carter & Bulik, 1994; Carter, Bulik, McIntosh and Joyce, 2002; Jansen, 1998).

The context-potentiated eating effect reported here and in Petrovich *et al*. (2007) agrees with Jansen's model. People who restrain food consumption can eat in a specific context (e.g., at home) and after several pairings, the context can elicit overeating.

Furthermore, according to the present results, high density caloric food rather than low density caloric food, might promote a stronger context-nutrients association which then could lead to overeating. On the other hand, Petrovich *et al*. (2007) have suggested that the context-nutrients association elicits cravings for food paired with the context rather than a more general motivation to eat.

These results, taken together, suggest that those cues paired with high density caloric food could become effective CSs, which will elicit a craving for the specific high density caloric food. According to this idea, Alpers & Tuschen-Caffier (2004) found that individuals who exhibit binge eating behaviour tend to eat high density caloric food during their binges, whereas during non-binge meals they generally consume fewer calories than healthy controls.

The present study should be evaluated within the context of learning processes. Our results point out the relevance of both contextual conditioning and caloric density of food to explain binge behaviour in rats. Nevertheless, it remains unclear to which extent other biological factors are also implicated in binge eating.

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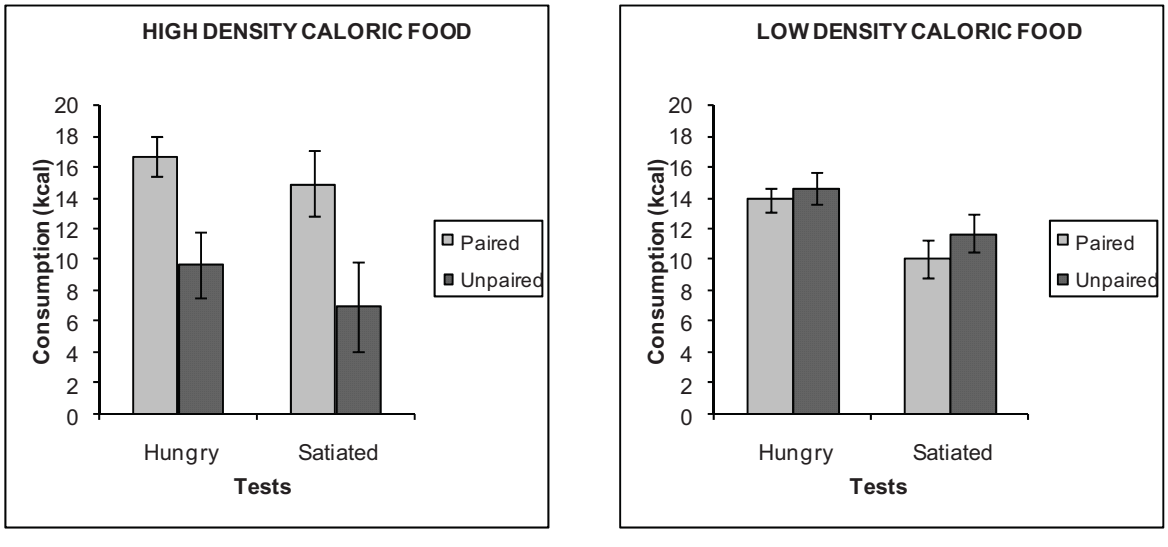
FIGURE CAPTIONS

Figure 1. Groups mean intake (±SEs) in kcal for High-density caloric groups (on the left) and Low-density caloric groups (on the right) during hungry and satiated tests. Paired = groups tested in the conditioned context; Unpaired = groups tested in the non conditioned context.



8.5. Study 5

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ASSOCIATION OF INDIVIDUAL AND FAMILY EATING PATTERNS DURING CHILDHOOD AND EARLY ADOLESCENCE: A MULTICENTER EUROPEAN STUDY OF ASSOCIATED EATING DISORDER FACTORS

INTRODUCTION

Recent studies have indicated that unhealthy eating pattern early in life (Micali, Holliday, Karwautz, Haidvogel, Wagner, Fernandez-Aranda, Badia, Gimenez, Solano, Brecelj-Anderluh, Collier, Treasure, in press) and parental influence upon children's eating styles (Birch, Fisher, Grimm-Thomas, Markey, Sawyer, Johnson, 2003) can be part of the developmental trajectory into eating disorders (EDs). Nevertheless, it should be acknowledged that little previous research has addressed this topic, and that the few findings that have been reported have been conflicting and have suffered from several fundamental shortcomings. The Fifth European Framework on healthy eating has established a collaboration of eight countries with the aim to overcome these limitations and to examine the individual and environmental factors associated with the development of EDs.

OBJECTIVES

To examine whether individual and family eating patterns and food choices during childhood and early adolescence were associated with disordered eating behaviors and weight (assessed through Body Mass Index (BMI).

HYPOTHESIS

We hypothesized that compared to the control sample, patients with EDs would exhibit more problematic eating behaviors early in life and that the family of these patients would exhibit more dysfunctional eating behaviors early in life and that the family of these patients would exhibit more dysfunctional eating behaviors and attitudes towards food than the family members of the controls.

METHOD

A total of 261 ED patients (33.5% [N=88] an, 47.2%[N=123] with BN and 19.3% [N=50] with EDNOS) and 160 healthy controls.
ED cases were referred for assessment and treatment to our unit diagnosed according to DSM-IV criteria.
Healthy controls with similar demographic features to the clinical participants were recruited from individuals visiting the hospital for routine blood tests and were asked to volunteer in a study of environmental factors associated with the development of EDs.

ASSESSMENT

Participants completed the Early Eating Environmental Subscales of the Cross-Cultural (Environmental) Questionnaire (CCQ), a retrospective measure, which has been developed as part of a European Multicenter trial in order to detect dimensions associated with EDs in different countries. In the control group, also the GHQ-28, the SCID-I interview and the EAT-26 were used.

RESULTS

During childhood and early adolescence, the following main factors were identified to be linked to EDs:

- ☆ eating excessive sweets and snacks
- ☆ consuming food specially prepared for the respondent
- ☆ Conversely regular breakfast consumption was negatively associated with an ED.

CONCLUSIONS

Compared to healthy controls, ED patients report unfavorable eating patterns early in life, which in conjunction with an excessive importance given to food by the individual and the family may increase the likelihood for developing a subsequent ED.

Table 1: Sociodemographical features of the ED patients and the controls

Table 2: Logistic regression (adjusted by sex and age): effect of food style on the disorder.

Table 3: Logistic regression (adjusted by sex and age): effect of food style on the BMI

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Research Report

Individual and family eating patterns during childhood and early adolescence: An analysis of associated eating disorder factors

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Abstract

To examine whether there is an association between individual and family eating patterns during childhood and the likelihood of developing an eating disorder (ED) later in life. The sample comprised 261 eating disorder patients [33.5% [$N = 88$] anorexia nervosa (AN), 47.2% [$N = 123$] with bulimia nervosa (BN) and 19.3% [$N = 50$] with Eating Disorders Not Otherwise Specified (EDNOS)] and 160 healthy controls from the Province of Catalonia, Spain, who were matched for age and education. All patients were consecutively admitted to our Psychiatry Department and were diagnosed according to DSM-IV criteria. Participants completed the Early Eating Environmental Subscale of the Cross-Cultural (Environmental) Questionnaire (CCQ), a retrospective measure of childhood eating attitudes and behaviours. In the control group, also the General Health Questionnaire-28 (GHQ-28) was used. During childhood and early adolescence, the following main factors were identified to be linked to eating disorders: eating excessive sweets and snacks and consuming food specially prepared for the respondent. Conversely, regular breakfast consumption was negatively associated with an eating disorder. Compared to healthy controls, eating disorder patients report unfavourable eating patterns early in life, which in conjunction with an excessive importance given to food by the individual and the family may increase the likelihood for developing a subsequent eating disorder.

Keywords: Eating disorders; Eating patterns; Anorexia nervosa; Bulimia nervosa; Eating disorders not otherwise specified

Introduction

A recent systematic review of the risk factor literature suggested that early eating and gastrointestinal difficulties may be developmental factors of relevance for eating disorders (Jacobi, Hayward, de Zwaan, Kraemer, & Agras, 2004). Early problematic eating patterns (e.g. struggle and conflict over eating) are associated with unhealthy eating behaviours later in the development (Kortegaard, Hoerder, Joergensen, Gillberg, & Kyvik, 2001). In a retrospective study comparing 51 teenage participants with anorexia nervosa (AN) and 51 controls, extreme feeding problems were more commonly reported by mothers of individuals with AN than of controls (Gillberg, Gillberg, Rastam, & Johansson, 1996).

Early childhood eating and problems for bulimia nervosa (BN) have been contradictory. While one study (Micali et al.[1]) of sister discordant for eating disorders found that cases of BN were more often overweight with

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[1]Micali, N., Holliday, J., Karwautz, A., Haidvogel, M., Wagner, G., Fernandez-Aranda, F., Badia, A., Gimenez, L., Solano, R., Breceli-Anderluh, M., Collier, D., & Treasure, J. L. (Accepted for publication). Developmental risk factors in eating disorders-childhood feeding and weight: A discordant sister-pairs comparison. *Psychotherapy and Psychosomatics*.

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less picky eating in childhood compared to their healthy siblings during childhood, Marchi and Cohen's (1990) study indicated that pica, early digestive difficulties and weight loss attempts were associated with subsequent bulimic behaviours. It should however be acknowledged that the research into early patterns of eating behaviour has been limited as the size of prospective longitudinal studies is rarely large enough to have sufficient power to be confident in the findings for eating disorders and the detail about the form of early eating risk may be insufficient.

Family eating patterns during childhood and early adolescence

Research has shown that children's attitudes toward food and children's evaluation of satiety are influenced by their parents and their family environment. Parents provide access to foods in the home, may operate as models and offer encouragement/discouragement for specific eating behaviours (Birch & Fisher, 1998; Birch et al., 2001). Accordingly, great difficulties over control issues between parents and children at mealtimes has often been linked to problematic food consumption in children, weight fluctuations and concerns about food, all of which could in turn result in an eating disorder later in the individual's development (Birch & Fisher, 1998). However research has not yet addressed whether distinct parental attitudes to food are associated to different eating disorder subtypes.

An integrative model for risk factors in eating disorders

Previously, risk factors for eating disorders have been proposed mainly from a particular theoretical viewpoint (e.g. biological, psychodynamic model, cognitive-behavioural), but not so commonly from an integrative standpoint (e.g. biopsychosocial model) (Jacobi et al., 2004). Yet, important developments in the level of understanding of the causes of complex disorders such as psychiatric problems is the recognition that simple unidimensional models of aetiology such as for instance genetic factors (Ribases et al., 2004, 2006) are insufficient and that rather complex models with interactions between a genetic predisposition and environmental precipitants may be necessary (Bulik, Sullivan, & Kendler, 2003; Karwautz et al., 2001). Interesting examples of research which have used such a paradigm have revealed that the short (inactive) form of the MAOI in combination with early adversity is associated with conduct disorder (Caspi et al., 2002) and that the short (inactive) form of the serotonin reuptake (5HTT) in combination with stressful life events leads to depression (Caspi et al., 2003). In order for this type of approach to be adopted in the field of eating disorders it is important to have tools, which clearly define the environmental risk factors of relevance. For this reason, effective prevention and treatment programmes require clear evidence-based models of aetiology.

Taken together the literature suggests that an unhealthy eating pattern early in life and parental influence upon children's eating styles can be part of the developmental trajectory into eating disorders. Nevertheless, it should be acknowledged that little previous research has addressed this topic, and that the few findings that have been reported have been conflicting. Furthermore preceding research has suffered from several fundamental shortcomings, including small sample sizes, lack of control groups, insufficient information on the methodology employed. Moreover, the reported risk factors are based on only a few studies mostly conducted with individuals from Anglo-Saxon populations and therefore their level of classification may vary with the appearance of more recent studies. For this reason, replication studies are required for the majority of the categorized risk factors.

Aims of the study

The aim of the present study therefore was to overcome the limitations of the previous studies by employing a large sample size of patients and healthy controls. Moreover, the present study aimed to develop an instrument, sensitive to the environmental factors associated with the development of eating disorders, which could be used in studies of gene environment interaction and to examine this instrument as a tool to measure related factors in individuals with eating disorders.

The specific objectives were to examine whether individual and family eating patterns and food choices during childhood and early adolescence were associated with disordered eating behaviours and weight (assessed through Body Mass Index [BMI]). We hypothesized that compared to the control sample, patients with eating disorders would exhibit more problematic eating behaviours early in life and that the family of these patients would exhibit more dysfunctional eating behaviours and attitudes towards food than the family members of the controls.

Method

Participants

The present study employed a case-control design. Entry into the study was between March 2001 and September 2002. The sample comprised 261 eating disorder patients (33.5% [$N = 88$] AN, 47.2% [$N = 123$] with BN and 19.3% [$N = 50$] with EDNOS) and 160 healthy controls. All clinical participants were diagnosed according to DSM-IV criteria (APA, 1994), using a semi-structured clinical interview [SCID-I] (First, Gibbon, Spitzer, & Williams, 1996), conducted by experienced psychologists and psychiatrists. All interviewers were trained in the administration of the SCID-I, although formal interrater reliability was not computed for this study. Clinical participants were consecutive referrals for assessment and treatment at the Department of Psychiatry of the University Hospital of Bellvitge in Barcelona.

The mean age of the total sample was 25.1 years (SD = 5.6). Age did not differ significantly between the

eating disordered patients and the controls (ED cohort: mean = 24.8, SD = 5.6; control group: 25.6, SD = 5.5; $p = 0.62$). However, the two groups differed on gender, with the eating disorder group comprising significantly more females than the control group (ED cohort: female = 93.89%; control group: female = 85.53%; $p = 0.02$). Furthermore in comparison to the control group, significantly more eating disorder patients were employed (ED cohort: employed = 62.45; control group: employed = 45.75; $p = 0.006$). The BMI of the patients differed between the groups, as would be expected with the AN group exhibiting the lowest BMI (mean = 16.8; SD = 1.95) and those with BN the highest BMI (mean = 23.3, SD = 4.49; $p = <0.0005$). Most of the participants had grown up in urban areas (75.3%).

The mean duration of the eating disorder group was 6.37 years (SD = 4.77). The mean number of previous treatments was 0.82 (SD = 0.91). They reported a weekly average of 4.13 binges (SD = 5.62) and 6.58 vomiting episodes (SD = 8.84). The inclusion criteria for the study for the eating disorder sample were: (a) older than 18 years, (c) meeting DSMIV-TR criteria (APA, 2000a) for AN, BN or for EDNOS. Conversely, patients were excluded from the study if they met any of the following criteria: (a) missing values for any diagnostic items; (b) unable to complete the assessment because of cognitive impairment; or, (c) current psychotic disorder. For the present analysis, the following individuals had to be excluded from an initial sample of 283 patients: (a) patients ($N = 18$) with missing values for any diagnostic tools; (b) cognitive impairment ($N = 2$); (c) comorbid psychotic disorder ($N = 2$). Disposition decisions were made by psychologists or psychiatrists who completed the anamnesis together with the treatment team according to published treatment guidelines (APA, 2000b).

Healthy controls were recruited from individuals visiting the hospital for routine blood tests and were asked to volunteer in a study of environmental factors associated with the development of eating disorders. All controls were from the same catchment areas as index patients. The final control group included 160 volunteers who were matched for age and education. The exclusion criteria for the control group were: (a) younger than 18 years; (b) to have lifetime history of health or mental illnesses (including eating disorders), screened by the General Health Questionnaire-28 (Goldberg, 1981) and the DSM-IV criteria (APA, 1994). From an initial sample of 166 controls, 6 participants were excluded, who had had a lifetime eating disorder.

All participants provided informed consent and the study was approved by the Ethics committee of our University Hospital.

Assessment

The early Eating Environmental Subscale of the Cross-Cultural (Environmental) Questionnaire (CCQ)

This retrospective self-administered questionnaire entails a total of 51 items. It was developed by an expert group from various European countries in order to detect environmental factors associated with the development of eating disorders (childhood eating patterns, meaning and value of food, family style, independence, parenting, self-development and social ideals of thinness and fitness and activity). The CCQ was based on the major instruments in the field of eating disorders, which are the Oxford Risk Factor Interview (Fairburn et al., 1998; Fairburn, Welch, Doll, Davies, & O'Connor, 1997) and the McKnight Risk Factor Interview (Shisslak et al., 1999). We were particularly interested to include items of these domains that might be sensitive to differences within the European cultures. The questionnaire was initially piloted in several patients and amended in the interest of clarity and coherence. In the current study, only the 16 items of the food and eating family style domain were considered. These items were developed following focus groups of patients with eating disorders who were asked about their early eating behaviours (i.e. before age 12) from the UK and Spain and from a consensus meeting of expert clinician group from Spain, the UK, Italy, Austria, Finland, Slovenia and France (Healthy Eating Consortium) after a review of the literature and the major eating disorder risk factor instruments. The instrument is shown in the Appendix and a copy of the whole questionnaire can be requested from the first author.

Reliability of the CCQ

The internal consistency of the derived scales fluctuated between good and very good (Cronbach α coefficients between 0, 75 and 0, 88). The dimensional scores derived from the factorial analysis discriminated adequately between patients and controls ($p \leqslant 0.05$) and the global diagnostic capacity of the test was found to be satisfactory (area below the ROC curve $\geqslant 0.80$) (Bonillo, Granero, Krug, Anderluh, Bellodi, Collier, Karwautz, Nacmias, Treasure & Fernandez-Aranda)[2]. Test–retest reliability was measured through κ coefficients (for categorical items) and intraclass correlation coefficients (for quantitative items) for the domain assessed in this study. A very high agreement, with an average value of 0.92 (95% confidence interval: 0.89–0.93) was found for all the items.

General Health Questionnaire-28 [GHQ-28] (Goldberg, 1981)

The GHQ-28 is a self-report questionnaire that has been designed to detect and assess individuals with an enlarged probability of a present psychiatric disorder. The GHQ-28 comprises four subscales: Somatic Symptoms, Anxiety and Insomnia, Social Dysfunction, and Severe Depression. In the current study, the Likert scoring procedure (0–3) was

[2]Bonillo, A., Granero, R., Krug, I., Anderluh, M., Bellodi, L., Collier, D. A., et al. (2006). Psychometric Reliability and Validity of the Cross-Cultural (Environmental) Questionnaire (CCQ). In *Poster presented at the Hispano Latinoamericano Congress on eating disorders*, 6th June, Barcelona.

used. An SPSS computer code was utilized to score the GHQ-28, which generated new variables. A cut off score of 6/7 (6 = no case; 7 = case) was employed for the new total subscale variables in order to exclude individuals with an elevated likelihood of a present psychiatric disorder. In previous studies this cut off score has yielded a sensitivity of 76.9% and a specify of 90.2% (Lobo, Perez-Echeverria, & Artal, 1986; Molina et al., 2006).

In addition, the eating disorder group was assessed by a face-to-face structured clinical interview regarding their eating disorder and psychopathological symptoms and their family history of eating disorders (Fernandez-Aranda & Turon, 1998; First et al., 1996).

Procedure

Upon presentation at the eating disorders unit, experienced psychologists and psychiatrists conducted a 2 h structured diagnostic face to face interview to measure eating disorder symptoms and psychopathological traits. Eating-disorder diagnoses were based on this interview and were consensually derived among members of the clinical team who had participated in the assessment. Finally, participants completed the questionnaires individually in a room prior to starting the treatment. For the control group, screening for a current or lifetime eating disorder and/or general distress was measured by self-report with the GHQ-28 (Goldberg, 1981) and eating disorder DSM-IV criteria (APA, 1994). An information sheet at the start of the questionnaire informed the participants about the purpose of the study and assured confidentiality of the results. Furthermore, it was emphasized that participation in the study was completely voluntary and that participants were free to withdraw from the study at any time.

Statistical analysis

The statistical analysis was carried out with the SPSS program, version 12 for Windows. All significance tests were two-tailed. Primarily, various multiple logistic regression models were conducted. These models assessed the extent to which different eating patterns during childhood and early adolescence (independent variables) could predict the presence or not of a subsequent eating disorder (dependent variable). Moreover, differential analyses were carried out to distinguish between the different types of diagnoses, whereby each disorder was compared with the control group. Our aim was to choose the best model. This was an exploratory analysis and therefore a wide group of predictors was employed using automatic sequential procedures for the input (entry) and output (exit) of variables (backstep and forwardstep procedures). The selected models, which had been controlled for sex and age, included all the predictors that were significant ($p<0.05$) or marginally significant ($p<0.10$). The models' ability to discriminate between the groups was also assessed with the area under the receiver operator curve (ROC). The models' calibration was examined using the Hosmer and Lemeshow test. Finally, Nagelkerke R^2 was used to estimate how much variance was accounted for in the models. Secondly, multiple linear regression models were carried out to determine which factors of the food style (independent variables) could best predict the participants' BMI (dependent variable). These analyses also used automatic sequential procedures for the input–output of the variables and were also controlled for sex and age. Diverse models were obtained for the different DSM-IV diagnoses (APA, 1994) and the control group. The global predictive capacity of the selected models was valued with the adjusted R^2 coefficient.

Results

The effect of individual and family eating patterns on eating disorders

Table 1 demonstrates the results of the four models, which measure the effect of eating patterns during childhood and adolescence on the presence of an eating disorder later in life. The first model (dependent variable: controls versus cases), indicates that living with a sibling(s) increases the incidence of having an eating disorder (OR = 2.14, 95% CI: 1.01–4.52). This occurrence is augmented when food was specially prepared for the respondent (OR = 6.46) and when participants ate fatty/sugary snacks (OR = 1.99 if the frequency was for eating 2/6 times a week and OR = 3.85 for a daily frequency). On the other hand, having the first meal of the day before attending school lessons (not skipping breakfast) diminished the incidence of developing an eating disorder (OR = 1/0.298 = 3.36). The results of the second model (dependent variable: controls versus people with AN), indicate that the occurrence of AN is increased when grandparent(s) lived at home (OR = 2.09), when food was specially prepared for the respondent (OR = 7.52) and when the children ate a lot of fatty/sugary snacks (OR = 2.06 for eating moderately and OR = 4.01 for eating a lot). There was a trend for children with restricted access to salty/sugary snacks to have a lower incidence of presenting AN (OR = 1/0.464 = 2.16).

The third model (dependent variable: controls versus people with BN) found that the associated BN factors are: food prepared specially for the respondent (OR = 4.81), and eating a lot of fatty/sugary snacks (OR = 1.94 if the frequency was for eating 2/6 times a week and OR = 3.15 for a daily frequency). Having the first meal of the day before attending school lessons was however found to reduce this occurrence (OR = 1/0.247 = 4.05). Fathers appeared to have an impact on the increased incidence of BN. For example fathers with a greater value placed on food augmented the likelihood (OR = 2.30) for BN and there was a trend for fathers' attention to healthy eating to increase the occurrence.

The final model (dependent variable: controls versus EDNOS) shows that the incidence of presenting an

Table 1
Logistic regression (adjusted by sex and age): effect of food style on the disorder

Independent variables	*B*	*P*	e^B	95% CI	For e^B	Adjustment[a]
Model: controls versus cases ($N = 421$)						
Sibling(s) lived at home	0.760	0.046	2.138	1.01	4.52	AUC = 0.732
Grandparent(s) lived at home	0.489	0.086	1.631	0.93	2.85	H–L = 0.641
Had first meal of day before lessons	−1.212	0.001	0.298	0.15	0.59	$R^2 = 0.215$
Food prepared specially for respondent	1.865	0.004	6.455	1.83	22.73	
Father valued food more than others	0.567	0.028	1.763	1.06	2.92	
Freq. ate fatty/sugary snacks (1)[b]	0.689	0.006	1.992	1.22	3.26	
Freq. ate fatty/sugary snacks (2)[c]	1.349	0.001	3.853	1.89	7.86	
Model: controls versus anorexics ($N = 243$)						
Grandparent(s) lived at home	0.735	0.038	2.086	1.04	4.19	AUC = 0.736
Food prepared specially for respondent	2.017	0.004	7.518	1.87	30.17	H–L = 0.143
Freq. ate fatty/sugary snacks (1)	0.723	0.043	2.060	1.02	4.15	$R^2 = 0.223$
Freq. ate fatty/sugary snacks (2)	1.391	0.002	4.018	1.67	9.65	
Restricted access to salty/sugary snacks	−0.767	0.087	0.464	0.19	1.12	
Model: controls versus bulimics ($N = 277$)						
Had first meal of day before lessons	−1.397	0.001	0.247	0.12	0.53	AUC = 0.763
Food prepared specially for respondent	1.571	0.041	4.810	1.07	21.70	H–L = 0.235
Father valued food more than others	0.831	0.008	2.295	1.24	4.26	$R^2 = 0.248$
Father paid attention to healthy eating	1.583	0.081	4.871	0.83	28.76	
Freq. ate fatty/sugary snacks (1)[b]	0.664	0.040	1.943	1.03	3.67	
Freq. ate fatty/sugary snacks (2)[c]	1.148	0.009	3.152	1.34	7.42	
Model: controls versus EDNOS ($N = 208$)						
Ate meals together less than 3 times/day	0.803	0.042	2.231	1.03	4.83	AUC = 0.700
Had first meal of day before lessons	−1.367	0.004	0.255	0.10	0.65	H–L = 0.571
Restricted access to salty/sugary snacks	−1.124	0.050	0.325	0.11	1.00	$R^2 = 0.146$

[a]AUC = area under the ROC curve; H–L = Hosmer and Lemeshow test; R^2 = Nagelkerke R^2.
[b]Frequency ate fatty/sugary snacks (1): 2–6 times a week versus never or less than once a week.
[c]Frequency ate fatty/sugary snacks (2): Every day versus never or less than once a week.

EDNOS increases when participants consumed meals less than three times a day (OR = 2.23). Again the factors related to a reduced likelihood were eating breakfast before school lessons OR = 1/0.255 = 3.92 and having restricted access to salty/sugary snacks (OR = 1/0.325 = 3.08).

All the models included in Table 1 demonstrated a good ability to discriminate between the groups. This can be seen in the fact that the area under the receiver operator curve is over 0.70. Moreover, the adjustment was correct in all cases (values $p > 0.05$ in the Hosmer and Lemeshow tests). The total variance accounted for in the models was between 15% (controls versus EDNOS) and 25% (controls versus BN).

The effect of individual and family eating patterns on the BMI

Table 2 contains the linear regression models that evaluate the effect of eating pattern variables on the person's later BMI. We have obtained different regression equations for samples with diverse body compositions. In one group, the model could not be controlled for due to the lack of participants (there were only 14 non-purgative BN patients in the study).

The results of the models showed that only a few independent variables were statistically associated with the BMI. Since the adjusted R^2 coefficients vary between 6% and 16%, the eating pattern factors included in the study explain only a small part of the variance of this criterion. This result suggests that these models should be interpreted with caution. The EDNOS sample is the only exception, since in this case the R^2 value was found to be 71%. According to the results of this model, the EDNOS participants who lived together with sibling(s) had a lower BMI ($B = -1.83$, 95%; CI: −3.61 to −0.04).

For the rest of the models, the most notable results indicate that the BMI is bigger if: food was used as a reward, food was specially prepared for the grandparent, the father and the respondent, a high number of family members were present at meals and there was a shortage of luxury food in the family. Contrarily, the model shows that the BMI decreases when the access to food was restricted (punishment) and sibling(s) lived at home.

Discussion

The instrument that we have developed appears to be sensitive to the food-related environmental factors that might be associated with the development of an eating disorder. The significant sociodemografical findings (more females and more women employed in the clinical group than in the control group) could be a spurious finding. The

Table 2
Linear regression (adjusted by sex and age): effect of food style on the BMI

Independent variables	*B*	*P*	95% CI	For *B*
Model: cases and controls sample, $R^2 = 0.073$ ($N = 461$)				
Only few times meals were included in social events	1.105	0.034	0.09	2.13
Shortage of luxury foods in family	1.415	0.037	0.09	2.74
Model: case sample, $R^2 = 0.120$ ($N = 261$)				
Less than 3 times/day ate meals together after 12 years	2.288	0.006	0.67	3.91
Food prepared specially for grandparent	1.986	0.055	−0.05	4.02
Food prepared specially for father	3.215	0.020	0.52	5.91
Only few times meals were included in social events	1.350	0.082	−1.74	2.87
Model: anorexic sample, $R^2 = 0.098$ ($N = 83$)				
Less than 3 times/day ate meals together after 12 years	0.974	0.064	−0.06	2.01
Food was used as a reward	1.245	0.033	0.10	2.39
Model: restricted anorexic sample, $R^2 = 0.117$ ($N = 42$)				
Number of family members present at meals	0.810	0.040	0.04	1.58
Model: purgative anorexic sample, $R^2 = 0.073$ ($N = 41$)				
Restricted access to food (punishment)	−1.91	0.038	−3.70	−0.12
Model: bulimic sample, $R^2 = 0.164$ ($N = 117$)				
Less than 3 times/day ate meals together after 12 years	2.539	0.021	0.40	4.68
Food prepared specially for respondent	3.209	0.073	−0.31	6.73
Food was used as a reward	1.774	0.060	−0.08	3.62
Model: purgative bulimic sample, $R^2 = 0.104$ ($N = 103$)				
Food prepared specially for grandparent	2.173	0.085	−0.31	4.65
Model: non-purgative bulimic sample				
Small sample				
Model: EDNOS sample, $R^2 = 0.706$ ($N = 48$)				
Sibling(s) lived at home	−1.826	0.045	−3.61	−0.04
Model: purgative sample, $R^2 = 0.059$ ($N = 144$)				
Food prepared specially for grandparent	2.974	0.021	0.46	5.49
Model: non anorexic sample				
No variables were significant				
Model: control sample				
No variables were significant				

R^2 = adjusted R^2 coefficient.

likelihood of developing any form of eating disorder was diminished by eating breakfast and increased by eating snacks and having food specially prepared for the respondent, but also by the fathers' value on food. No significant differences between eating disorder subcategories appeared in our study on these variables.

Skipping breakfast and excessive ingestion of sweets and snacks

In the present study, the two specific eating patterns, that might be related to a later eating disorder, were: skipping breakfast and consuming excessively sweets and snacks before the age of 12. Skipping breakfast is often employed as a weight reduction method on nutritional intake among young women (Barker, Robinson, Wilman, & Barker, 2000; Belderson et al., 2003; Lattimore & Halford, 2003). Lattimore and Halford (2003) for instance found that women who were dieting to lose weight were three times more likely to skip breakfast than females who were not dieting. Breakfast skipping has also often been documented to be related to other adverse lifestyle habits such as smoking, alcohol use, low exercise and obesity (Keski-Rahkonen, Kaprio, Rissanen, Virkkunen, & Rose, 2003). The excessive ingestion of sweets and snacks may be linked to the conflict and difficulties around meals or problematic eating that have been found in various longitudinal risk factor studies (Kortegaard et al., 2001; Kotler, Cohen, Davies, Pine, & Walsh, 2001).

Fathers' attitudes to food

Furthermore, the fathers' attitudes towards food may be associated with the development of a later eating disorder (namelly BN) in their daughters. Studies in support of our findings have for instance indicated that eating disordered

females recounted a poor father–daughter relationship (Botta & Dumlao, 2002), lower paternal care (Palmer & Treasure, 1999), less paternal empathy (Steiger, Fraenkel, & Leichner, 1989) and overprotection (Berger et al., 1995; Lavik, Clausen, & Pedersen, 1991; Waller, Slade, & Calam, 1990). Furthermore, in a longitudinal risk factor study maladaptive paternal attitudes (not related to food and weight) were linked to the risk of developing an eating disorder (Johnson, Cohen, Kasen, & Brook, 2002). On the other hand, other studies revealed that eating disorder patients reported feeling closer to their fathers than to their mothers (Kent & Clopton, 1992). Accordingly, further studies have indicated that while mothers' and daughters' perceptions of family functioning differed significantly (Dancyger, Fornari, & Sunday, 2006), they did not differ significantly between fathers and daughters (Dancyger, Fornari, Scionti, Wisotsky, & Sunday, 2005).

Coming from a large family and living with grandparents at home

Two other social factors that were found in this study and might be related to an increased occurrence of eating disorders were coming from a large family and living with grandparents at home. These factors might be country specific, as they have not been previously mentioned in other studies. Meal patterns are related to socio-economic structure, work schedules, life course, living conditions and feeding styles, as shown in previous studies (Birch & Fisher, 1998; Cullen, Baranowski, Rittenberry, & Olvera, 2000; Neumark-Sztainer, Story, Perry, & Casey, 1999). Thus parents increasingly have to rely on the grandparents' help to bring up their children. The present findings could have resulted from inadequate feeding styles (permissive vs. not flexible) employed by grandparents. Research has shown that authoritarian feeding was related to lower ingestion of fruit, juices, and vegetables (Birch & Fisher, 1998; Cullen et al., 2000). However, it should be noted that eating disorders have multifactorial causes and that this might only be one out of many contributing factors (Bulik et al., 2003). Further validation of the relationship between living with other family members and the development of a subsequent eating disorder is therefore required.

Eating patterns and BMI

The last but not least finding of our study was that some eating patterns during childhood and early adolescence might be associated with an increased BMI, especially not having regular meal patterns and using food as a reward. This result is in concordance with previous eating disorder studies (Killen et al., 1996; Patton, Selzer, Coffey, Carlin, & Wolfe, 1999). Similar findings have also been observed in obesity, where a positive relationship between skipping breakfast and lifetime obesity in children has been revealed (Berkey, Rockett, Gillman, Field, & Colditz, 2003; Pastore, Fisher, & Friedman, 1996; Summerbell, Moody, Shanks, Stock, & Geissler, 1996).

This study has some limitations that do not permit a direct generalization of the present results. First, the retrospective and self-report data collection procedures may have limited the validity and the reliability of our findings, which are subject to unreliability of individual recall and potential memory bias. Set against this are the high values obtained on the test–retest reliability of the procedure. Furthermore, given the retrospective design of the study, it could also be that other factors, which have not been considered in this study might be related to early childhood feeding problems and the development of a subsequent eating disorder. Second, the cross-sectional design does not allow us to determine causality of the variables assessed, since we do not know the direction of the association—for e.g. it could be that those who develop an eating disorder remember their breakfast or weight or other details in a different way than those who do not have an eating disorder.

Future research could expand these results employing longitudinal designs addressing the potential mediating role of individual and family eating patterns in the etiological factors and clinical course of eating disorders. Furthermore, forthcoming research could examine whether the people with a particular genotype and common psychosocial factors (as those studied here), are more vulnerable for developing an eating disorder.

Our findings suggest that if programs to improve childhood and adolescent eating patterns are to be successful, they need to focus on a wide range of environmental factors. In particular, the family should be informed about the importance of structuring meal times with shared meals particularly breakfast and increasing the accessibility and promotion of snacks. Furthermore, maintaining structured family meals might encourage healthier diets in children and adolescents and could also allow the family to gain a better understanding of the child's food choices. Finally, the social interaction at meal times may promote children to experience eating constructively and could therefore help in creating positive attitudes towards food, which could persist into later years.

In conclusion, the findings from the present study agree with the growing body of research indicating that a variety of environmental and social factors are associated with unhealthy individual and family eating patterns during childhood and early adolescence and which if not detected early could result in the development of a subsequent eating disorder.

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Appendix

Section 3: Individual and family eating patterns

(5) During your childhood, which family members, and how many family memebers were living in your home? (tick appropriate boxes)?

		Lived at home		Number
		Yes (1)	No (0)	
a	Father			
b	Mother			
c	Sibling(s)			
d	Step-mother/father			
e	Step/half-sibling(s)			
f	Aunt/Uncle			
g	Grandparent(s)			
h	Other			

(6) During your childhood, how many family members would be present at most meals?_____

(7) How often did you eat meals together as a family (children plus at least one parent/care-giver) *before* you were 12 and *after* you were 12 when you were living at home (*please tick*)?

		3 times a day (0)	1-2 times a day (1)	2-7 times a week (2)	Once a week or less (3)
a	Before you were 12				
b	After you were 12 and living at home				

(8) Before you were 12, did you usually eat meals at regular set times of the day (*tick one*)?
☐ Yes ☐ No

(9) Before you were 12, did you usually have your first meal of the day before school/lessons started?
☐ Yes ☐ No

(10) Before you were 12, how often would you eat meals an fast food franchised restaurants, McDonalds etc. (*tick one*)?

Never	
Once a month or less	
1-4 times a month	
At least once a week	

(11) During your childhood, did anyone in your family have food prepared specially for them on a regular basis (e.g. due to a physical illness, different taste)?

		Yes (1)	No (0)
a	Grandparent		
b	Mother		
c	Father		
d	Sibling		
e	Yourself		
f	Other household member/care-giver		

(12) During your childhood, how much value was put on food by your mother and/or your father (*tick as applicable*)?

		An average amount or less value than most people (0)	More value than most people (1)	A lot more value than most people (2)
a	Mother			
b	Father			

(13) During your childhood, did anyone in the family pay specific attention to healthy eating, such that it had a profound effect on the food that was eaten in your family (*tick as appropriate*)?

		Yes (1)	No (0)
a	Mother		
b	Father		
c	Sibling		
d	You		
e	Other household member/caregiver		

(14) During your childhood, how often were meals included as an important part of social events in your extended family or among your family's friends and how often were you included in these meals?

		Once a week or more (0)	1-4 times a month (1)	5-8 times a year (2)	2-4 times a year (3)	Less than twice a year (4)
a	Frequency of 'social' meals					
b	Frequency of inclusion in 'social' meals					

(15) Compared to your friends, did your parents have strict rules about the times of food you ate as a child?
☐ Yes ☐ No

(16) If yes, how often did you follow these rules (*tick one*)?

Never	
Occasionally	
Frequently	
Always	

(17) How often did you eat fatty or sugary snacks (e.g. crisps, chocolate, sweets, sugary fizzy drinks) as a child?

Never	
Less than once a week	
2-6 times a week	
Every day (less than 3 times)	
Every day (3 or more times)	

(18) Was your access to fatty or sugary snacks restricted, compared to your friends?
☐ Yes ☐ No

(19) How often did your family use food as a reward (e.g. for good behaviour) and how often did your family restrict your access to food as a form of punishment (*tick one*)?

		Never (0)	Occasionally (1)	Frequently (2)
a	Food used as a reward			
b	Food access restricted as a form of punishment			

(20) During your childhood, was there ever a shortage of food in your family (*if yes, please indicate type of food*)?

		Yes (1)	No (0)
a	Shortage of basic foods		
b	Shortage of luxury foods		

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8.6. Study 6

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Treasure, J.,
Anderluh, M.,
Bellodi, L.,
Cellini, E.,
Collier, D.,
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Granero, R.,
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ASSOCIATION OF INDIVIDUAL AND FAMILY EATING PATTERNS DURING CHILDHOOD AND EARLY ADOLESCENCE: A MULTICENTER EUROPEAN STUDY OF ASSOCIATED EATING DISORDER FACTORS

Recent studies have indicated that unhealthy eating pattern early in life (Micali, Holliday, Karwautz, Haidvogel, Wagner, Fernandez-Aranda, Badia, Gimenez, Solano, Breceli-Anderluh, Collier, Treasure, in press) and parental influence upon children's eating styles (Birch, Fisher, Grimm-Thomas, Markey, Sawyer, Johnson, 2003) can be part of the developmental trajectory into eating disorders (EDs). Nevertheless, it should be acknowledged that little previous research has addressed this topic, and that the few findings that have been reported have been conflicting and have suffered from several fundamental shortcomings. The Fifth European Framework on healthy eating has established a collaboration of eight countries with the aim to overcome these limitations and to examine the individual and environmental factors associated with the development of EDs.

Figure 1. Map of Europe

OBJECTIVES

1.) to examine in more detail some of the early patterns of eating behavior which may be associated with the development of a subsequent ED.

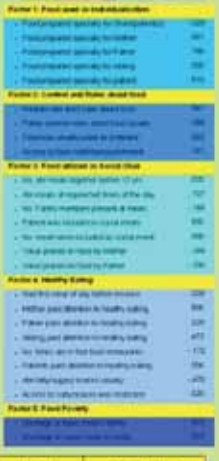
2.) to assess whether there were differences across countries in these early putative associated eating behaviors.

3.) to evaluate whether there were differences among the distinct ED sub diagnosis n early individual and family eating behavior

METHOD

A total of 1664 participants took part in the present study. ED cases (n= 879) were referred for assessment and treatment to specialized ED units in five different European countries (Spain, Austria, Italia, Slovenia and the UK) diagnosed according to DSM-IV criteria. Healthy controls (n=785) with similar demographic features to the clinical participants were ascertained from various community sources from the same catchment area.

Table 1. Factor loading in CatPCA procedures in the European clinical sample



ASSESSMENT

Participants completed the Early Eating Environmental Subscales of the Cross- Cultural (Environmental) Questionnaire (CCQ), a retrospective measure, which has been developed as part of a European Multicenter trial in order to detect dimensions associated with EDs in different countries. In the control group, also the GHQ-28, the SCID-I interview and the EAT-26 were used.

RESULTADOS

Five individually CatPCA analyses were adjusted, one for each theoretically expected factor. Logistic regression analyses indicated that the domains with the strongest effects from the CatPCA scores in the total sample were:

1) food used as individualization

2) control and rules about food

3) food used as social glue

4) healthy eating

5.) food poverty

☆ In the total European sample, higher scores in factors 1 and 2 increased the likelihood of suffering from an ED.

☆ On the other hand lower scores in the factor healthy eating were negatively related to the development of a subsequent ED.

☆ When differences between countries were assessed, results indicated that the pattern of associated ED factors did vary between countries.

☆ There was very little differences in early eating behavior on the subtypes of ED.

Table 2. Predictive accuracy of empirical factors scores on the presence of an ED diagnosis for the total European Sample and each country

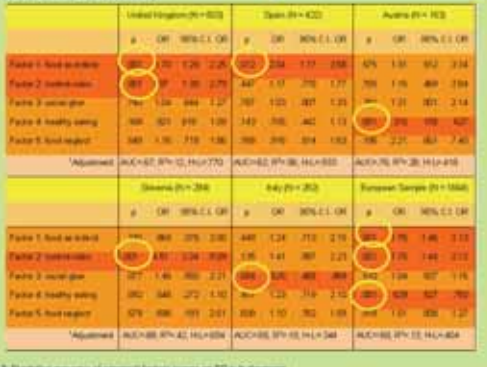


Table 3. Predictive accuracy of empirical factors scores on ED sub diagnosis

CONCLUSIONS

These findings suggest that the fragmentation of meals within the family and an excessive importance given to food by the individual and the family are linked to the later development of an ED.

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Associations of individual and family eating patterns during childhood and early adolescence: a multicentre European study of associated eating disorder factors

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The objective of this study was to examine whether there is an association between individual and family eating patterns during childhood and early adolescence and the likelihood of developing a subsequent eating disorder (ED). A total of 1664 participants took part in the study. The ED cases (*n* 879) were referred for assessment and treatment to specialized ED units in five different European countries and were compared to a control group of healthy individuals (*n* 785). Participants completed the Early Eating Environmental Subscale of the Cross-Cultural (Environmental) Questionnaire, a retrospective measure, which has been developed as part of a European multicentre trial in order to detect dimensions associated with ED in different countries. In the control group, also the General Health Questionnaire-28 (GHQ-28), the semi-structured clinical interview (SCID-I) and the Eating Attitudes Test (EAT-26) were used. Five individually Categorical Principal Components Analysis (CatPCA) procedures were adjusted, one for each theoretically expected factor. Logistic regression analyses indicated that the domains with the strongest effects from the CatPCA scores in the total sample were: food used as individualization, and control and rules about food. On the other hand, healthy eating was negatively related to a subsequent ED. When differences between countries were assessed, results indicated that the pattern of associated ED factors did vary between countries. There was very little difference in early eating behaviour on the subtypes of ED. These findings suggest that the fragmentation of meals within the family and an excessive importance given to food by the individual and the family are linked to the later development of an ED.

Eating disorders: Eating problems: Eating behaviour: Adolescence: Anorexia nervosa: Bulimia nervosa: Childhood: Family

A recent systematic review of the risk factor literature suggested that early eating and gastrointestinal difficulties may be developmental factors of relevance for eating disorders (ED)[1]. However, research into early patterns of eating behaviour has been limited as the size of prospective studies has rarely been large enough to have sufficient power to be confident in the findings for ED and the detail about the form of early eating risk may be insufficient[2–7].

Individual eating patterns during childhood and early adolescence

Research has shown that eating behaviours in childhood do appear to be linked to the later development of ED[8–10]. The two longitudinal studies addressing this topic reported that early problematic eating patterns are associated with subsequent unhealthy eating behaviours[11,12] and that

Abbreviations: AN, anorexia nervosa; AUC, area under the receiver operator curve; BN, bulimia nervosa; CatPCA, Categorical Principal Components Analysis; EAT-26, Eating Attitudes Test; ED, eating disorder; EDNOS, eating disorders not otherwise specified; GHQ-28, General Health Questionnaire-28; SCID-I, semi-structured clinical interview.

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eating conflicts and struggles around meals increased the risk of anorexia nervosa (AN) later in life, whereas eating too little protected against the development of bulimia nervosa (BN)[13].

Several retrospective studies on AN and BN have also addressed this issue[10,14]. Even though this type of design has limitations, it can nevertheless be used to explore and define potential risk factors. In relation to AN, studies have indicated that compared to controls, mothers of individuals with AN reported more extreme feeding problems and severe gastrointestinal problems of their children during infancy[14,15]. Early childhood eating and problems for BN have been contradictory. While one study[10] of sister discordant for ED found that BN individuals were more often overweight with less picky eating and eating more quickly during infancy than their healthy siblings, Marchi & Cohen[12] revealed that pica, early digestive difficulties and weight-loss attempts were related to subsequent bulimic behaviours. Further studies are therefore needed to clarify these inconsistencies.

Family eating patterns during childhood and early adolescence

Research has shown that children's attitudes towards food and children's evaluation of satiety and appetite are influenced by their parents and their family environment[16,17]. Parents control the food environment and operate as models for eating and food-related behaviours. In relation to ED, research on the effects of familial factors on problematic eating behaviours in childhood has not frequently been examined[18]. The few findings in this field have been contradictory with some studies indicating that a restrictive feeding style by parents was related to the development of overweight in their children[19]. In contrast, parental control over eating was related to eating fewer meals and snacking less frequently[20]. Moreover, critical comments about eating, weight and shape from family members have been found to be associated with bulimic forms of ED[21,22]. However, research has not yet addressed whether distinct parental attitudes to food are associated with different ED subtypes.

Cultural influences on eating disorders

Cultural differences in individual and family eating styles and whether these might impact on the development of ED has rarely been addressed. It is, nevertheless, generally accepted that food preferences are culturally learned and that different countries have their own distinct diets and attitudes towards food[23–25]. Sociocultural factors are important contributing factors in the development of ED[1,26,27]. This is particularly relevant for the bulimic disorders which suddenly emerged in cohorts born after 1950 in the USA and Western Europe[26]. In spite of this, research in this area has predominantly assessed ethnic minority groups residing in the UK[28] or the USA[29–31]. There have been fewer comparisons of environmental risk factors between countries and even fewer across Europe[32–34].

To summarize, the confidence that can be placed in findings from the literature on early risk factors for ED is limited. The few studies that have addressed this topic have yielded conflicting results. The scope of possible risk factors is limited as are the outcomes used. Nonetheless, there is some evidence to suggest that the development of unhealthy eating attitudes and behaviours in early childhood and parental influence upon children's eating styles can be part of the developmental trajectory into ED.

Aims of the study

The overall aim of the present study was to recruit a large sample of patients and healthy controls from the range of environments within Europe. Our specific objectives were: (1) to examine in more detail some of the early patterns of eating behaviour which may be associated with the development of a subsequent ED; (2) to assess whether there were differences across countries in these early putative associated eating behaviours; (3) to evaluate whether there were differences among the distinct ED sub-diagnoses in early individual and family eating behaviour; and (4) whether these differed between the different countries. We hypothesized that unhealthy individual and family eating styles in childhood and early adolescence would be related to an ED later in life and that ED sub-diagnoses and countries would differ in these associated eating behaviours.

Methods

Participants

The present study employed a case-control design. Six centres from five different European countries (two for Italy) participated in the current study: the University Hospital of Bellvitge, Barcelona, Spain (ED, *n* 262, control, *n* 160); the Medical University of Vienna; Department of Child and Adolescent Psychiatry (ED, *n* 94, control, *n* 59); the Eating Disorders Research Unit, Institute of Psychiatry, London, UK (ED, *n* 319, control, *n* 184); the Department of Neurology and Psychiatric Services, University of Florence, Italy (ED, *n* 50, control, *n* 50); the Department of Psychiatry, Fondazione Centro del Monte Tabor, Milan, Italy (ED, *n* 93, control, *n* 101) and the University Psychiatric Hospital, University of Ljubljana, Slovenia (ED, *n* 61, control, *n* 231). Entry into the study was between March 2001 and September 2002. The total sample comprised 1664 participants, 879 ED patients [42·2 % with AN, 32·2 % with BN and 25·6 % with eating disorders not otherwise specified (EDNOS)] and 785 healthy controls. Considering the ED sub-diagnoses, we found that 52·8 % of the AN patients were diagnosed with the restrictive subtype and 47·2 % with the bulimic-purgative subtype. This distribution was statistically equal for countries ($P=0·071$). Due to the limited sample size of non-purging BN individuals a distinction between purging and non-purging BN subtypes could not be made.

Most ED participants were ascertained from the participating clinical sites and the remaining individuals were collected from different therapeutic institutions for ED, self-help groups, announcements in the mass media and on ED conferences. Participants were ill at assessment and were diagnosed according to DSM-IV-R[35] criteria, using a semi-structured clinical interview (SCID-I)[36] or EATAET (M Anderluh *et al.*, unpublished results; only used for Austria and the UK), carried out by experienced psychologists and psychiatrists.

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The interviewers were trained in the administration of these instruments although formal inter-rater reliability was not computed for the present study. The exclusion criteria for the ED patients in the present study were: (1) individuals who had not completed a diagnostic assessment; (2) younger than 16 years old; (3) unable to complete the assessment because of cognitive impairment and/or serious medical condition; or (4) current psychotic disorder. For the present analysis, the following ED individuals had to be excluded from an initial sample of 901 patients: (1) patients (*n* 18) did not have a diagnosis measured; (2) cognitive impairment (*n* 2); (3) comorbid psychotic disorder (*n* 2).

Healthy controls (*n* 785) with similar demographic features (sex, age and education) to the clinical participants were ascertained from various community sources from the same catchment area. The exclusion criteria for the control group were: (1) younger than 16 years; (2) a lifetime history of ED was assessed by the General Health Questionnaire-28[37], the SCID-I[36] according to DSM-IV-R criteria[35] and the Eating Attitudes Test (EAT-26)[38] (total score >20). From the initial sample of 791 controls, six participants were excluded, who had had a lifetime ED. Ethical approval for the study was obtained from the relevant committees at each site.

The mean age of the total sample was 25·3 (SD 8·7) years. The ED patients were significantly older than the controls (ED cohort: mean 26·7 (SD 8·9) years; control group: mean 23·8 (SD 8·2); $P=0·001$). The gender ratio also differed, the ED group comprised significantly more females than the control group [ED cohort: female 96·4 %; control group: female 91·1 %; $P=0·001$). Also more ED patients were employed (ED cohort: employed 54·9 %; control group: employed 39·1 %; $P=0·001$) whereas more controls were currently studying (ED cohort: student 47·80 %; control group: student 75·32 %; $P=0·001$), which might be attributable to the lower age in the control group. More ED cases had grown up in urban places (ED cohort: urban 68·97 %; control group: urban 56·78 %; $P=0·001$). More than half of the sample came from families with one or more sisters (58·07 %) and had advanced education (54·53 %). The mean age of onset of the ED was 19·32 (SD 5·05) years and the mean duration of the disorder was 7·11 (SD 5·44) years. The median of previous treatments was 1 (ranging from 0 to 5). Participants reported a weekly average of 4·8 (SD 5·8) binge eating episodes and 7·1 (SD 8·7) vomiting episodes. Their mean BMI at assessment was 20·44 (SD 6·53) kg/m^2.

Assessment

The Early Eating Environmental Subscale of the Cross-Cultural (Environmental) Questionnaire. This retrospective self-administered questionnaire has fifty-one items with six subscales. It was developed by an expert group from various European countries in order to detect environmental factors associated with the development of ED (childhood eating patterns, meaning and value of food, family style, independence, parenting, self-development and social ideals of thinness and fitness and activity). The Cross-Cultural (Environmental) Questionnaire was based on the major instruments in the field of ED, which are the Oxford Risk Factor Interview[21–39] and the McKnight Risk Factor Interview[40]. The internal consistency of the derived scales fluctuated between good and very good (Cronbach's α coefficients between 0·75 and 0·88). The dimensional scores derived from the factor analysis discriminated adequately between patients and controls ($P\leq 0·05$) and the global diagnostic capacity of the test was found to be satisfactory (area under the receiver operator curve (AUC) $\geq 0·80$)[42].

The items for the eating section of the questionnaire were developed from a focus group with patients and following a review of the literature with an expert group of clinicians. The items generated by this process were then grouped into themes by three expert clinicians. There were five theoretical domains: food used as individualization, control and rules about food, food utilized as social glue, healthy eating and food deprivation. In the current study, only twenty-six of the twenty-nine items of the food and eating family style subscale were considered. Two items were not included due to the lack of cases with positive answers ('food prepared specially for others' and 'specific attention to healthy eating by others'). Moreover, another item was excluded because it measured current instead of childhood eating patterns ('eat meals together after 12 years'). A detailed description and a copy of this subscale can be found in another recent publication and can be requested from the corresponding author[8]. A very high agreement, with an average value of 0·92 (95 % CI 0·89, 0·93) was found for all the items.

EATATE Phenotype Interview. The EATATE interview was developed for the European Healthy Eating Project. It is a semi-structured interview, comprising a European adaptation of the Longitudinal Interval Follow-up Evaluation[42] and the Eating Disorders Examination[43]. The interview is used to obtain a life-time history of ED symptoms, which are then plotted on a lifeline. This instrument has been validated and has demonstrated good inter-rater reliability in terms of diagnoses (0·82–1·0) and illness history variables (0·80–0·99) (M Anderluh *et al.*, unpublished results).

General Health Questionnaire. The General Health Questionnaire-28 (GHQ-28)[37] is a self-report questionnaire that has been designed to detect and assess individuals with an enlarged probability of a present psychiatric disorder. The GHQ-28 has been studied in various European countries and was found to be a valid and reliable tool[44].

Eating Attitudes Test. The EAT-26[38] assesses a broad range of symptoms and provides a total score for disturbed eating attitudes and behaviour. This instrument has acceptable criterion related validity with Cronbach's α ranging from 0·82 to 0·89 in a previous study.

Procedure

Participants were invited to participate in a European multicentre study. All patients were first assessed by board-certified psychologists or psychiatrists using a 2 h structured diagnostic face-to-face or phone interview to measure ED symptoms and psychopathological traits. ED diagnoses were based on this interview and were consensually derived among members of the clinical team who had participated in the assessment. An information sheet at the start of the questionnaire informed the participants about the purpose of the study and assured confidentiality of the results.

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Furthermore, it was emphasized that participation in the study was completely voluntary and that participants were free to withdraw from the study at any time.

Statistical analysis

Statistical analysis was carried out with SPSS version 15.0.1 for Windows (SPSS Inc., Chicago, IL, USA). Firstly, through the Categorical Principal Components Analysis (CatPCA) procedure, we obtained an empirical reduction of the set of twenty-six variables which make up the early eating subscale included in the analysis. This method is included in the optimal scaling procedures and can be used for uncovering the underlying structure (factors or dimensions) of a large set of variables; therefore it reduces the income of a large set of variables to a reduced number of underlying factors. It is adequate for variables with mixed scaling levels (including nominal levels) and it assumes that the relationship among observed variables is not linear. CatPCA was carried out in the whole European clinical sample (n 879). Five individually CatPCA analyses were adjusted, one for each theoretically expected factor. In each analysis the number of dimensions was fixed *a priori* at one (one-dimensional solution). First, we obtained and interpreted the factor or component loadings, which represent the correlation coefficients between the original income variables and the new factors that emerged. Next, factor scores of each dimension were obtained for each participant. In the context of principal component analysis, a factor score is a numerical value which indicates a person's relative spacing or standing on the latent emerged factor. In the present study, factor scores were computed including all the items analysed in each model, independently of its factor loading since in this work content is considered more important than reliability[45]. The same coefficient matrix was used to calculate factor scores in the control sample.

Factor scores were compared between cases and controls for the total European sample and stratified by countries, with ANOVA procedures adjusted by sex and age. Next, the five empirical factor scores were included as independent variables into logistic and multinomial regressions (ENTER procedure) adjusted by sex and age to examine their predictive accuracy on the presence of an ED diagnosis (present *v.* absent, logistic regressions) and ED subtypes (absent–AN–BN–EDNOS, multinomial regressions). In the logistic models, significant OR higher than 1 indicate that higher factor scores increase the risk of suffering from an ED. In the multinomial models, the reference category was defined for the control group, and consequently significant OR higher than 1 indicate that higher factor scores increase the risk of reporting the concrete ED subtype. The global predictive accuracy of each model was valued with the Nagelkerke's R^2 coefficient and through the AUC. As it is commonly interpreted, we considered that AUC values between 0·60 and 0·70 are moderate, between 0·70 and 0·80 are good and above 0·80 are excellent. The adjustment was measured through Hosmer–Lemeshow's tests (P values higher than 0·05 are indicative of adequate adjustment). Independent models were constructed for data provided separately by each country and also for the total European sample.

Results

Results of the Categorical Principal Components Analysis procedure

Table 1 contains the factor loadings of each model obtained through the CatPCA procedures. Factor 1 was related to the theme of valuing food as a method of individualization (food specially prepared for family members), with especially high loadings for items measuring food prepared for father, sibling and the participant herself. Factor 2 was associated with the theme of control and rules about food, with the highest loadings for the items 'parents had strict rules about food', 'food was used as reward' and 'access to food restricted as punishment'. Factor 3 was linked to the employment of food as social glue and obtained the highest loadings for the two items 'patient was included in social meals' and 'number of foods included as a social event'. Factor 4 encompassed healthy eating, and it was especially associated with the parents', siblings' and the individual's own attention to healthy eating and also with restricted access to snacks and fast food. Factor 5 was associated with food deprivation and included the items shortage of basic and luxury food in the family (both with high factor loadings). A careful look at the items suggests that it could also reflect poverty or inadequate funds to buy foods in general or luxury foods specifically. The total variance explained by each factor was

Table 1. Factor loadings in Categorical Principal Components Analysis procedure in the European clinical sample (n 879)

	Component loadings
Factor 1: Food used as individualization	
Food prepared specially for grandparent(s)	−0·02
Food prepared specially for mother	0·09
Food prepared specially for father	0·80
Food prepared specially for sibling	0·83
Food prepared specially for patient	0·81
Factor 2: Control and rules about food	
Parents had strict rules about food	0·54
Follow parents' rules about food usually	−0·40
Food was usually used as a reward	0·68
Access to food restricted – punishment	0·74
Factor 3: Food utilized as social glue	
No. of times ate meals together before 12 years	0·03
Ate meals at regular/set times of the day	−0·11
No. of family members present at meals	−0·17
Patient was included in social meals	0·90
No. of meals were included as social event	0·91
Value placed on food by mother	−0·27
Value placed on food by father	−0·30
Factor 4: Healthy eating	
Had first meal of day (breakfast before school)	−0·04
Mother paid attention to healthy eating	0·60
Father paid attention to healthy eating	0·53
Sibling paid attention to healthy eating	0·47
No. of times ate in fast food restaurants	−0·17
Patients paid attention to healthy eating	0·56
Ate fatty/sugary snacks usually	−0·48
Access to salty/snacks was restricted	0·52
Factor 5: Food deprivation	
Shortage of basic food in family	0·82
Shortage of luxury foods in family	0·82

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satisfactory, with values ranging from 21·2 % (for factor 4, 'healthy eating') to 39·8 % (for factor 1, 'food used as individualization'). Reliability based on Cronbach's α values varied from moderate (0·49, for factor 5, 'food deprivation') to high (0·76, for factor 1, 'food used as individualization'). These results can be valued as adequate considering the reduced number of items contained in the factors.

The comparison of the frequency distribution for ED subtype (AN–BN–EDNOS) obtained some statistical associations. Concretely, food prepared specially for another sibling achieved a higher prevalence for AN patients (15·7 %) than for BN (7·5 %) or EDNOS (10·3 %) individuals (P=0·012). Considering the number of times that the respondent was included in 'social meals' (once a week or more), AN and EDNOS patients achieved higher percentages (11·5 and 13·6 %, respectively) than BN patients (4·8 %) (P=0·006). Compared to AN (11·8 %) and EDNOS (9·6 %), a higher percentage of BN patients (17·2 %) had mothers who valued food a lot more than most people (P=0·021). This trend was similar when the amount of value placed on food by the father was assessed (BN, 11·5 %; AN, 6·9 %; EDNOS, 5·2 %; P=0·002). Furthermore, results indicated that 25·2 % of BN patients, 13·9 % of EDNOS and 12·4 % of AN individuals did not have breakfast before going to school (P<0·0005). Finally, fast food restaurants were more frequently visited by EDNOS individuals (17·6 %) than by AN (13·9 %) and BN (10·3 %) patients (P=0·004).

Table 2 includes the frequency distribution (means and standard deviations) of the derived CatPCA factor scores for ED patients (cases) and controls. In the total European sample, ANOVA comparisons adjusted by sex and age indicated that cases obtained higher means in the factors 'food used as individualization' (P=0·001), 'control and rules about food' (P=0·001) and 'food deprivation' (P=0·007), and lower means in the factor 'healthy eating' (P=0·001); no differences between cases and controls were found for the factor 'food utilized as social glue'. Considering the country of origin, the first factor 'food used as individualization' obtained significant differences in the UK (P=0·001) and Spain (P=0·003). The second factor 'control and rules about food' obtained higher means in ED patients in the UK (P=0·001), Slovenia (P=0·001) and Italy (P=0·006). The third factor 'food utilized as social glue' differed significantly between ED cases and controls in Slovenia and Italy (P=0·001 in both samples). For the fourth factor, 'healthy eating', Austria (P=0·001) was the only country that was found to differ significantly between cases and controls. Finally, no significant differences between patients and controls were revealed for the fifth factor, 'Food deprivation'.

Association of the derived Categorical Principal Components Analysis factors and the presence of an eating disorder diagnosis

Table 3 contains the logistic models adjusted by sex and age that valued the predictive accuracy of the factor scores on the presence of an ED diagnosis. Considering the total European sample, higher scores in the factors 'food used as individualization' (OR 1·76) and 'control and rules about food' (OR 1·75) increased the likelihood of suffering from an ED. On the other hand, lower scores in the factor 'healthy eating' (OR 0·63) were negatively related to the development of a subsequent ED. This model obtained correct adjustment (P=0·404) and moderate predictive accuracy (R^2 0·13; AUC 0·68).

In the UK, the possibility of an ED was increased with higher scores in the factors 'food used as individualization' (OR 1·70) and 'control and rules about food' (OR 1·97). In the Spanish sample, the only statistical association with an ED diagnosis was for high scores in the factor 'food used as individualization' (OR 2·04). On the other hand, scores in the factor 'healthy eating' diminished the probability of developing an ED in Austria (OR 0·32), and the factor 'food utilized as social glue' was negatively related to an ED diagnosis in Italy (OR 0·63). In Slovenia, an ED diagnosis was positively related to scores in the factor 'control and rules

Table 2. Distribution for empirical factor scores in eating disorder cases and controls† (Mean values and standard deviations)

		UK (*n* 503)		Spain (*n* 422)		Austria (*n* 153)		Slovenia (*n* 294)		Italy (*n* 292)		Total (*n* 1664)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Factor 1	Cases	0·66	0·99	0·25	0·49	0·21	0·48	0·13	0·48	0·26	0·46	0·39	0·73
	Controls	0·25	0·66	0·12	0·30	0·25	0·46	0·16	0·43	0·19	0·44	0·19	0·48
	P value	0·00**		0·00**		0·64		0·67		0·19		0·00**	
Factor 2	Cases	0·51	0·61	0·04	0·55	0·00	0·47	0·31	0·61	0·48	0·60	0·30	0·62
	Controls	0·25	0·57	−0·03	0·51	−0·02	0·55	−0·04	·046	0·30	0·50	0·10	0·05
	P value	0·00**		0·15		0·79		0· 00**		0·01*		0·00**	
Factor 3	Cases	0·00	0·99	0·48	0·86	0·27	0·92	0·40	0·94	0·38	0·88	0·26	0·94
	Controls	−0·07	0·95	0·46	0·80	0·10	0·98	−0·06	0·94	0·74	0·71	0·21	0·93
	P value	0·45		0·89		0·28		0·00**		0·00**		0·27	
Factor 4	Cases	0·18	0·70	−0·18	0·48	0·10	0·68	0·27	0·54	−0·05	0·50	0·03	0·62
	Controls	0·18	0·75	−0·12	0·42	0·50	0·74	0·39	0·61	−0·15	0·43	0·14	0·64
	P value	0·92		0·23		0·00**		0·16		0·07		0·00**	
Factor 5	Cases	0·31	0·47	−0·17	0·36	0·25	0·42	0·15	0·32	0·64	0·71	0·30	0·50
	Controls	0·26	0·41	0·17	0·38	0·14	0·35	0·11	0·30	0·51	0·68	0·24	0·46
	P value	0·23		0·84		0·12		0·36		0·11		0·01*	

P values are based on ANOVA procedures adjusted by sex and age; two-sided significance level: *P<0·05, **P<0·01.
† For details of procedures and factors, see Methods and Table 1.

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Table 3. Predictive accuracy of empirical factor scores on the presence of an eating disorder diagnosis†

	UK (*n* 503)			Spain (*n* 422)			Austria (*n* 153)			Slovenia (*n* 294)			Italy (*n* 292)			European sample (*n* 1664)		
	P	OR	95 % CI OR	*P*	OR	95 % CI OR	*P*	OR	95 % CI OR	*P*	OR	95 % CI OR	*P*	OR	95 % CI OR	*P*	OR	95 % CI OR
Factor 1	0·00**	1·70	1·29, 2·25	0·01*	2·04	1·17, 3·58	0·58	1·31	0·51, 3·34	0·74	0·87	0·38, 2·00	0·45	1·24	0·71, 2·15	0·00**	1·76	1·46, 2·13
Factor 2	0·00**	1·97	1·39, 2·79	0·45	1·17	0·78, 1·77	0·76	1·15	0·47, 2·84	0·00**	4·51	2·24, 9·09	0·14	1·41	0·90, 2·23	0·00**	1·75	1·44, 2·12
Factor 3	0·74	1·04	0·84, 1·27	0·79	1·03	0·81, 1·33	0·28	1·31	0·80, 2·14	0·08*	1·46	0·96, 2·21	0·00**	0·63	0·46, 0·86	0·51	1·04	0·93, 1·16
Factor 4	0·17	0·82	0·62, 1·09	0·14	0·71	0·44, 1·13	0·00**	0·32	0·16, 0·63	0·09*	0·55	0·27, 1·10	0·45	1·23	0·72, 2·10	0·00**	0·63	0·53, 0·75
Factor 5	0·55	1·16	0·71, 1·86	0·77	0·92	0·51, 1·63	0·20	2·21	0·66, 7·40	0·58	0·70	0·19, 2·51	0·61	1·10	0·76, 1·59	0·92	1·01	0·81, 1·27
Adjustment	AUC 0·67; R^2 0·01; H–L 0·77			AUC 0·62; R^2 0·06; H–L 0·93			AUC 0·76; R^2 0·28; H–L 0·42			AUC 0·88; R^2 0·42; H–L 0·69			AUC 0·65; R^2 0·10; H–L 0·34			AUC 0·68; R^2 0·13; H–L 0·40		

AUC, area under the receiver operator curve; H–L, Hosmer–Lemeshow test (*P* value); R^2, Nagelkerke's R^2.
Logistic regression models (ENTER procedure), adjusted by sex and age; two-sided significance level: *$P<0·05$, **$P<0·01$.
† For details of procedures and factors, see Methods and Table 1.

about food' (OR 4·51). All the independent models for countries included in Table 3 obtained correct adjustment ($P>0·05$ in Hosmer–Lemeshow's tests). The most predictive models corresponded to Slovenia (R^2 0·42; AUC 0·88) and Austria (R^2 0·28; AUC 0·76).

Association of the derived Categorical Principal Components Analysis factors and the presence of an eating disorder subtype

Table 4 shows the multinomial logistic regression models adjusted by sex and age that valued the predictive accuracy of factor scores on the presence of a concrete ED subtype. The Slovenian sample was omitted in this analysis due the lack of information of the subtype diagnosis for these patients. In the total European sample, the factors increasing the likelihood of any subtype (AN, BN and EDNOS) were 'food used as individualization' and 'control and rules about food', and the factor negatively related to all ED subtypes was 'healthy eating'. This model obtained moderate predictive accuracy (R^2 0·136).

Considering the country of origin, 'food used as individualization' increased the incidence of all ED subtypes in the UK. In Spain, this factor was also positively related to the development of AN and BN. The factor 'control and rules about food' augmented the probability of presenting AN and BN in the UK and of developing BN in Italy. Conversely, 'food utilized as social glue' decreased the likelihood of developing AN in Italy. The factor 'healthy eating' diminished the occurrence of AN in Spain, and it was also negatively related to AN and EDNOS in Austria. On the contrary, in Italy 'healthy eating' increased the probability of developing BN. Finally, the factor 'food deprivation' was negatively related to AN in Spain. The predictive accuracy of the concrete models for each country was moderate, and ranged between R^2 0·096 for Spain to R^2 0·372 for Austria.

Discussion

The instrument that was employed in the present study seems to be sensitive to the food-related environmental factors that might be related to the development of a subsequent ED. In the total sample we found that the five domains established through the CatPCA were of relevance although most of these were of small effects. In accordance with our first hypothesis, we found that the domains 'food used as individualization' and 'control and rules about food' increased the probability of developing a later ED. Contrastingly, 'healthy eating' was found to be negatively associated with a subsequent ED. Furthermore, as hypothesized, some differences across countries were reported. Finally, in relation to our third and fourth aim only a few differences were observed for the derived CatPCA dimensions across ED sub-diagnoses, the total European sample and the distinct countries. The present unexpected results could to some extent have resulted from the low predictive capacity reported in most of the assessed models.

Food as individualization

In relation to our first aim, which examined whether some of the early patterns of eating behaviour were related to the development of a subsequent ED, we revealed that 'food

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Table 4. Predictive accuracy of empirical factor scores on eating disorder subtypes†

		Anorexia			Bulimia			EDNOS		
		P	OR	95% CI OR	*P*	OR	95% CI OR	*P*	OR	95% CI OR
UK (*n* 503; R^2 0·132)	Factor 1	0·02*	1·46	1·06, 2·00	0·01*	1·67	1·12, 2·48	0·00**	2·00	1·47, 2·72
	Factor 2	0·00**	2·08	1·38, 3·13	0·00**	3·58	1·97, 6·53	0·07*	1·50	0·97, 2·31
	Factor 3	0·73	1·04	0·82, 1·33	0·64	1·09	0·75, 1·58	0·95	1·01	0·78, 1·30
	Factor 4	0·12	0·77	0·55, 1·08	0·37	0·80	0·48, 1·31	0·54	0·90	0·63, 1·27
	Factor 5	0·79	1·08	0·61, 1·92	0·95	0·97	0·42, 2·24	0·36	1·31	0·73, 2·32
Spain (*n* 422; R^2 0·096)	Factor 1	0·01*	2·55	1·29, 5·04	0·05*	1·92	1·01, 3·65	0·17	1·69	0·80, 3·60
	Factor 2	0·80	1·08	0·61, 1·92	0·57	1·15	0·71, 1·88	0·31	1·34	0·76, 2·34
	Factor 3	0·95	1·00	0·71, 1·39	0·95	0·99	0·73, 1·34	0·39	1·18	0·81, 1·70
	Factor 4	0·03*	0·45	0·22, 0·92	0·73	0·91	0·52, 1·58	0·31	0·70	0·35, 1·39
	Factor 5	0·03*	0·27	0·08, 0·89	0·40	1·32	0·69, 2·56	0·93	1·04	0·45, 2·36
Austria (*n* 153; R^2 0·372)	Factor 1	0·80	1·17	0·33, 4·11	0·45	0·41	0·04, 4·18	0·15	2·39	0·74, 7·76
	Factor 2	0·79	0·83	0·21, 3·26	0·44	1·64	0·46, 5·78	0·64	1·34	0·40, 4·48
	Factor 3	0·66	1·16	0·60, 2·23	0·17	1·83	0·78, 4·29	0·66	1·17	0·58, 2·39
	Factor 4	0·02*	0·29	0·10, 0·82	0·08*	0·41	0·15, 1·13	0·01*	0·24	0·09, 0·65
	Factor 5	0·72	1·38	0·24, 8·04	0·50	1·81	0·32, 10·2	0·07*	3·97	0·91, 17·3
Italy (*n* 292; R^2 0·186)	Factor 1	0·06*	1·79	0·97, 3·30	0·15	0·50	0·20, 1·28	0·35	1·92	0·50, 7·40
	Factor 2	0·50	1·21	0·69, 2·13	0·03*	1·90	1·07, 3·33	0·40	0·55	0·13, 2·26
	Factor 3	0·00**	0·55	0·37, 0·80	0·12	0·71	0·47, 1·09	0·32	0·67	0·31, 1·46
	Factor 4	0·68	0·87	0·44, 1·69	0·03*	2·11	1·07, 4·16	0·51	0·59	0·12, 2·84
	Factor 5	0·77	0·94	0·59, 1·48	0·42	1·22	0·75, 2·00	0·28	1·62	0·67, 3·90
European sample (*n* 1370; R^2 0·136)	Factor 1	0·00*	1·81	1·44, 2·28	0·01*	1·45	1·11, 1·90	0·00**	2·34	1·85, 2·97
	Factor 2	0·00**	1·82	1·42, 2·33	0·00**	1·86	1·42, 2·43	0·01*	1·48	1·12, 1·97
	Factor 3	0·58	0·96	0·83, 1·11	0·11	1·15	0·97, 1·37	0·84	0·98	0·83, 1·17
	Factor 4	0·00**	0·51	0·41, 0·66	0·00**	0·62	0·48, 0·81	0·00*	0·66	0·51, 0·86
	Factor 5	0·77	0·96	0·71, 1·29	0·16	1·25	0·92, 1·70	0·88	1·03	0·74, 1·43

EDNOS, eating disorders not otherwise specified; R^2, Nagelkerke's coefficient.
Multinomial regressions (ENTER procedure) adjusted by sex and age (reference category: control group); two-sided significance level: *$P<0·05$, **$P<0·01$.
† For details of procedures and factors, see Methods and Table 1. Data from Slovenia are not included due the lack of diagnose subtype in this sample.

used as individualization' was positively associated with a later ED. The need for individualized foods within the family (father, siblings and own patients) might be related to the increased risk of ED within the family by decreasing social bonding. However, it could also be a marker of multiple domains, and could measure the importance of food for individualization and perhaps respect within the family or it could also be a measure of picky eating as shown in previous studies[10,12]. In accordance with the present findings, previous research has indicated that adolescents who struggled for autonomy, disliked food served at family meals and often refused to attend family meals[16,46]. However, other studies have documented that regardless of their longing for independence and experimentation, adolescents ultimately slipped back to favour the same foods as their parents[47]. More demanding lifestyles, such as extended working and school hours, increased after-school activities, transformations in family and living arrangements, and augmented accessibility of convenience and fast foods could be responsible for an increased right to be special or different about food and its environment[48,49].

Control and rules about food

Another domain from the CatPCA that was found to increase the probability of presenting a later ED in the whole European sample was 'control and rules about food'. Previous studies have suggested that parents who employ food control strategies (e.g. reward, punishment or limiting access to certain foods) may actually discourage the formation of adequate control over eating in their children[50–52]. Also, research has shown that limiting access to food as a form of punishment was associated with an increased incidence of BN and binge ED. One hypothesis is that parents might restrict access to foods in response to their child's adiposity or snacking behaviour[19–50]. A second hypothesis is that mothers who themselves have eating problems may project their own control and rules about eating on to their offspring[10,20]. Only further longitudinal research will reveal the potentional mediating role of parental rules and control about food in the aetiological factors and clinical course of ED.

Healthy eating

The domain of 'healthy eating'(especially mother, father and own patient paid attention to healthy eating) from the CatPCA appeared to be negatively related to a later ED. In agreement with the present results, previous studies have also demonstrated that parents' modelling of optimal dietary behaviours was associated with children's intake of healthy foods and favourable eating patterns[53–55]. Healthy eating has also often been related to structured family meals, a high priority for family meals and an encouraging environment at family meals[56–61], and may contribute to a positive psychosocial development in children and adolescents[58,62,63].

Differences across countries in early eating behaviour

The secondary aim of the present study was to examine whether there were differences across countries in these

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early eating behaviours. The pattern of associated ED factors did vary between countries. In the UK and Spain, 'food used as individualization' was positively related to a later ED; 'control and rules about food' increased the incident of ED in the UK and Slovenia. In Austria 'healthy eating' was negatively related to an ED diagnosis and in Italy 'food utilized as social glue' diminished the incidence of ED.

Disparities in dietary habits across European populations may be related to different culutral norms, socio-economic differences, unstable political situations and variations in level of education achieved[64,65]. However, it should also be noted that even though there appear to be 'traditional cultures of eating habits' across EU countries, globally there are modern ones, such as 'fast food restaurants' which have started to enter our everyday life. Plotting such information on a timescale, documenting stable habitual eating habits *v.* new ones, would therefore be very important for nutrition research[66].

Our final two aims were to assess whether there were differences across ED sub-diagnoses for the total European sample and the distinct countries. In contrast to our expectations, we did not reveal differences in the assessed eating behaviours across ED sub-diagnoses. Similarly, when the distinct countries were assessed independently also only a few differences between ED sub-diagnoses emerged, which partially could be attributable to low statistical power.

Limitations and strengths of the present study

The present study has several limitations that need to be highlighted. The major limitation was that the instrument was retrospective. Therefore the risk and protective factors that we have defined are no more than retrospective correlates according to the criteria of Kraemer *et al.*[67]. Therefore it will be important to confirm the relevance of these factors in prospective studies. Furthermore, the case mix including a high proportion of clinical cases may have limited the validity and the reliability of the present findings. Also even though the detail about food and eating defined in this instrument was greater than in previous longitudinal studies, further definition and clarification is probably needed. For example, the meaning in translation of the value of food may lack precision. This may explain the lack of consistency in the link between ED and this item between countries. Nevertheless within a specific culture the meanings may be clear as exemplified by the high levels of test–retest reliability reported in a previous study[8]. Furthermore, it should be mentioned that feeding style is not just an environmental measure. Gene environment correlation highlights that the same individuals who provide our environment also provide us with our genes. Hence, some of the feeding practices seen in this paper could be correlated with genetically mediated characteristics of the parents that were unmeasured (e.g. parental ED, parental BMI). Finally, the sample sizes (for ED subtypes and control cohorts) and the success of the matching between controls and patients varied between the different countries, which affected the accuracy of the *P* values and the estimation in the regression models.

Notwithstanding these limitations, this is a large sample which has addressed early eating behaviours and the role of family values and attitudes in a standard way between different cultures in Europe. No previous study has relied on such a large sample. ED are low prevalence disorders, therefore any study aimed at clarifying risk factors for ED requires a large enough study. We were able to determine whether associated ED factors varied in each of the recruiting countries, due to the large sample size across the countries.

The findings from the present study may help to shape appropriate prevention and early intervention programmes, and identify 'at risk' (children and adolescent) individuals. The current findings indicate that nutritional policies and education should take into consideration that food and eating are influential manifestations of cultural and social identities and that these vary considerably across Europe. Such prevention efforts should include a variety of environmental factors such as informing the family to provide food within a structured context, to pay attention and monitor the youngster's eating patterns and to role-model healthy-eating practices[68,69].

The present study enhances our knowledge about the association between ED and unhealthy eating patterns in childhood and early adolescence, but several unanswered questions remain for future studies. Future research could expand the present results by employing longitudinal designs addressing the potential mediating role of individual and family eating patterns in the aetiological factors and clinical course of ED. Moreover, forthcoming research could examine whether the people with a particular genotype and common psychosocial factors (as those studied here) are more vulnerable for developing an ED and to determine how various risk factors interact in increasing the risk for disordered eating.

In conclusion, the present study focused on a variety of environmental and social eating-related factors in a large case control sample from various European countries, which are potentially modifiable early markers for ED. The findings from the present study agree with the growing body of research indicating that dysfunctional individual and family eating patterns in childhood and early adolescence could lead to the development of a subsequent ED. The present findings will therefore be imperative for developing models of risk using similar designs of populations from across Europe.

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8.7. Study 7

ANGER EXPRESSION IN EATING DISORDERS: CLINICAL, PSYCHOPATHOLOGICAL AND PERSONALITY CORRELATES

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INTRODUCTION

In eating disorders (EDs), anger and aggression are important psychopathologic traits (1), which have been found to be associated with ED subtype (1), severity of ED symptoms (2), comorbidity (3), altered biochemical functioning (4), endocrinological dysfunction (5), and poorer treatment outcome (6). Marked impulse dysregulation has also been associated with difficulties in expressing anger (7). The present study explores the manner in which various facets of anger are associated with ED symptoms, comorbid psychopathology, personality traits, and impulsive behaviours.

AIMS OF THE STUDY

- To compare various facets of anger expression in individuals with EDs and healthy controls.
- To explore the specific relation between anger and purging behavior.
- To explore the relation of anger expression to ED symptoms and general psychopathological features and personality traits.
- To determine the relation between anger expressions and self-damaging impulsive behaviors.

HYPOTHESIS

We hypothesized that:

- there would be higher scores on general anger expression in patients with EDs than controls.
- that patients with purging behaviour would score significantly higher on Anger-IN (a measure of anger suppression).
- that individuals with intense urges to express anger would also display a variety of impulsive self-destructive behaviours.

METHOD

COHORTS

- Clinical Group: N=135 ED Patients
- Control Group: N= 103 Healthy Controls

ASSESSMENT

- EAT- 40, EDI- 2, BITE, STAXI- 2, TCI-R — ED Symptomatology; Anger, Personality
- STAXI-2
- GHQ-28
- SCL-90-R, SAD, and other clinical and psychopathological indices — General Psychopathology; Social Avoidance

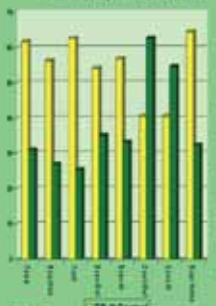
RESULTS

SPSS

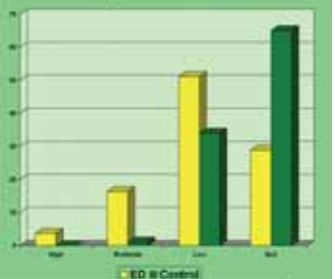
- Women with EDs score higher mean scores than the controls on all the STAXI-2 scores except for anger control ($p<0.05$).
- When various purging methods were assessed independently, the frequency of laxative use was associated with anger suppression ($p=0.03$).
- ED symptoms and specific personality traits were positively associated to different anger expressions ($p\leq0.05$).
- Anger Expression-Out are linked to decreased odds of suicide attempts (OR=0.98; $p=0.011$).
- Higher scores in Anger Control-Out are associated with decreased odds of compulsive buying (OR=0.97; $p=0.018$)
- Patients with higher scores on anger suppression were more likely to report self-harming behaviors ($p=0.001$).

Table 1: Sociodemographical and clinical features for the ED group.

Graph 1: Comparison of anger expression between ED patients and controls



Graph 2: Comparison of anger state between ED patients and controls



ED Control

Table 2: Logistic and linear regressions for exploring predictive value of anger on bulimic behaviors.

Table 3: Correlations between anger expressions and ED clinical and personality features.

DISCUSSION

ED patients may have inadequate anger expression and deficits in coping with anger and frustration. The relation between vomiting and various facets of anger is more complex than previously believed. Furthermore, different purging methods may be related to different facets of anger.

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Anger expression in eating disorders: Clinical, psychopathological and personality correlates

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Abstract

The goals of the study were to compare anger expressions in individuals with eating disorders and healthy controls and to explore the relation among eating disorder symptoms, comorbid psychopathology, personality traits, and impulsive behaviours. Participants comprised 135 eating disorder patients consecutively admitted to our unit and 103 healthy controls. Assessment measures included the Eating Disorders Inventory 2 (EDI-2), The Bulimic Investigatory Test Edinburgh (BITE), Symptom Checklist-Revised (SCL-90-R), Social Avoidance Distress Scale (SAD), Temperament and Character Inventory-Revised (TCI-R) and State-Trait Anger Expression Inventory 2 (STAXI-2) and other clinical and psychopathological indices. In the control group also the General Health Questionnaire-28 (GHQ-28) was used. Women with eating disorders obtained significantly higher mean scores than controls on all STAXI-2 scales except for Anger Control. When various purging methods were assessed independently, the frequency of laxative use was associated with anger suppression. Eating disorder symptoms and specific personality traits were positively associated to different anger expressions. Finally, patients with higher scores on anger suppression were more likely to report self-harming behaviors. Eating disorder patients may have inadequate anger expression and deficits in coping with anger and frustration. Furthermore, different purging methods may be related to different facets of anger.

Keywords: Anorexia nervosa; Bulimia nervosa; EDNOS; Severity; Aggressiveness; Impulsivity

1. Introduction

In eating disorders, anger and aggression are important psychopathologic traits (Fassino et al., 2001), which have been found to be associated with eating disorder subtype (Fassino et al., 2001), severity of eating disorder symptoms (Abbate-Daga et al., 2005), comorbidity (Fassino et al., 2003a), altered biochemical

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functioning (Coccaro et al., 1989), endocrinologic dysfunction (Bartolomucci et al., 2004; Coste et al., 2006) and poorer treatment outcome (Fava et al., 1995; Fassino et al., 2003b). Marked impulse dysregulation has also been related to difficulties in expressing anger (Tiller et al., 1995; Truglia et al., 2006). The present study explores the manner in which various facets of anger are linked to eating disorder symptoms, comorbid psychopathology, personality traits, and impulsive behaviors.

Aggressiveness can be defined as any behavior that is intended to harm. (Truglia et al., 2006). Research into the role of anger in eating disorders has been somewhat inconsistent and imprecise, which may in part be due to limits in the current conceptualization of this emotion. Generally anger was considered as a unitary construct (Arnow et al., 1995). However, Spielberger (1996) suggested that anger should be conceptualized as a multifaceted construct, comprising anger states (a changeable emotional condition consisting of subjective feelings of tension, annoyance, irritation, fury, or rage, frequently accompanied by the activation of the autonomic nervous system) and anger traits (an enduring personality feature, displaying individual differences in the incidence with which state anger is experienced over time). In addition, Spielberger remarked that individuals can differ in the ways in which they express or suppress their anger (Spielberger, 1996).

1.1. Anger and eating disorders

Little is known about the role that anger plays in eating disorders. The few studies assessing anger in eating disorders have generally revealed that individuals with eating disorders, especially bulimia nervosa (BN) patients, report higher anger levels than healthy controls (Fava et al., 1995; Tiller et al., 1995; Milligan and Waller, 2000; Fassino et al., 2001; Zaitsoff et al., 2002). Independent of diagnosis, elevated levels of unexpressed anger have been revealed in individuals with eating disorders (Milligan and Waller, 2000). More specifically, Arnow et al. (1995) outlined that anger plays a very important role in affect-driven overeating and bingeing. In relation to this, one unanswered question is whether severity of bulimic behaviors is related to higher levels of unexpressed anger, independent of diagnosis. The few studies that have addressed this topic have yielded contradictory findings with some studies indicating that anger outbursts were associated with greater severity of bulimic symptoms (Fava et al., 1995), while others found that individuals who vomited did not show more anger than those who did not vomit (Fassino et al., 2001; Abbate-Daga et al., 2005). Further research is needed to clarify these inconsistencies.

1.2. Anger and personality

An important dimension to consider when studying anger in eating disorders is the underlying personality traits (Fassino et al., 2001, 2002). Contrasting personality profiles reveal high harm avoidance, reward dependence, and low novelty seeking in individuals with anorexia nervosa (AN) and high impulsivity, sensation seeking and novelty seeking in individuals with bulimic presentations (Klump et al., 2000). To date, the few studies that have assessed anger and personality concurrently have not revealed replicable patterns of association between particular personality profiles and anger expression (Fassino et al., 2003a,c; Abbate-Daga et al., 2005); however; considerable room for further work in this area exists.

1.3. Anger and impulsivity

Impulsivity is the only trait that has consistently been found to be associated with anger and eating disorder symptoms. Various researchers have suggested that negative affective states (particularly anger) are strongly related to impulsive behaviors in eating disordered patients (Favaro and Santonastaso, 1999) such as suicidal and parasuicidal gestures (Rodriguez-Cano et al., 2006), self-injurious behavior (Grant et al., 2005) drug or alcohol abuse (Bulik et al., 2004), stealing (Grant and Kim, 2002), and sexual promiscuity (Wiederman et al., 1996; Matsunaga et al., 2000). Further validation of the relation between impulsivity and anger is required.

In sum, the research on anger in individuals with eating disorders is essential, since anger may have some etiological role and therefore could be a premorbid personality characteristic and/or a risk factor for developing eating disorders. Furthermore, high levels of anger may also be a barrier to treatment by maintaining psychopathology and should therefore be addressed in treatment (Fassino et al., 2002, 2003b).

The present study extends previous research on the association between eating disorders and anger by assessing whether the severity of bulimic features is related to anger expression. Taking a transdiagnostic approach rather than relying exclusively on diagnostic categories might allow us to understand why treatment outcome is not always directly related to the severity of bulimic symptoms and might also enable us to tailor treatment modules to specific needs of patients with deficits in particular areas. Furthermore, the detection of

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particular character and temperament traits and psychopathologic and impulsive cores in relation to anger expressions has not been assessed previously and is of great interest, as it may allow us to identify individuals who are at greater risk of developing severe clinical eating disorder symptoms.

1.4. Aims of the study

Given the current gaps in the literature, the goals of the present study were fourfold: (1) to compare various facets of anger expression in individuals with eating disorders and healthy controls; (2) to explore the specific relation between anger and bulimic behaviors; (3) to explore the relation of anger expression to eating disorder symptoms, general psychopathological features, and personality traits; (4) to determine the relation between anger expressions and self-damaging impulsive behaviors.

We hypothesized that there would be higher scores on general anger expression in patients with eating disorders than controls and that patients with bulimic behaviors would score significantly higher on Anger-In (a measure of anger suppression). Moreover, we hypothesized that individuals with intense urges to express anger would also display a variety of impulsive self-destructive behaviors.

2. Method

2.1. Participants

The present study employed a case-control design. Entry into the study was between January-2005 and March-2006. The total sample comprised 238 participants from the province of Catalonia. The mean age of the total sample was 25.15 (S.D.=5.7) years. Age did not differ significantly between the eating disordered patients and the controls (eating disorder cohort: mean=25.6, S.D.=6.7; controls cohort: 24.6, S.D.=4.3; $P=0.184$). The psychiatric cohort (the case group) included 135 eating disorder patients, who had consecutively attended the public outpatient primary mental-health service at the University Hospital of Bellvitge. In this group, 15.5% were diagnosed with AN, 55.6% with BN and 28.9% with eating disorder not otherwise specified (EDNOS). All patients met DSM-IV TR criteria (APA, 2000a) for these disorders. The majority of the patients were single (76.1%) and had completed secondary education (83.1%). Less than half the patients were employed (38.5%). The mean age of onset of the eating disorder was 18.8 years (S.D.=5) and the mean duration of the disorder was 6.6 years (S.D.=5). The mean number of previous treatments was 0.9 (S.D.=1). Participants reported a weekly average of 5.4 binge eating episodes (S.D.=7.5), 5.0 vomiting episodes (S.D.=7.8), 3.6 laxative use episodes (S.D.=7.4) and 1.0 diuretic use episodes (S.D.=4.8). Their mean BMI at assessment was 21.9 kg/m^2 (S.D.=15.1).

The exclusion criteria for the study for the eating disorder sample were: (a) male sex; (b) missing values for any diagnostic items (APA, 2000a); (c) unable to complete the assessment because of cognitive impairment; or, (d) current psychotic disorder. For the present analysis, the following individuals had to be excluded from an initial sample of 151 patients: a) males ($N=6$), as the number of males with these diagnoses was too small for meaningful comparisons; b) patients with missing values for any diagnostic tools ($N=8$) and (c) individuals with too many missing values on the assessment tools ($N=12$). Disposition decisions were made by psychologists or psychiatrists who completed the anamnesis together with the treatment team according to published treatment guidelines (Fernández-Aranda and Turon, 1998; APA, 2000b). From an initial sample of 135 controls the following individuals were excluded: a) males ($N=4$); b) participants who rejected the assessment ($N=23$) and c) individuals with a current psychiatric condition, screened by the GHQ-28 (Goldberg, 1981) ($N=5$). All participants provided informed consent and the study was approved by the Ethics committee of our University Hospital.

2.2. Assessment

2.2.1. Eating disorders inventory 2 (EDI-2; Garner, 1991)

This is a reliable and valid 91-item multidimensional self-report questionnaire that assesses different cognitive and behavioral characteristics, which are typical for eating disorders. The eleven subscales are: Drive for Thinness, Bulimia, Body Dissatisfaction, Ineffectiveness, Perfectionism, Interpersonal Distrust, Interoceptive Awareness, Maturity Fears, Asceticism, Impulse Regulation and Social Insecurity. This instrument was validated in a Spanish population (Garner, 1998) with a mean internal consistency of 0.63 (coefficient alpha).

2.2.2. The bulimic investigatory test Edinburgh (BITE; Henderson and Freeman, 1987)

This questionnaire contains 33 items that measures the presence and the severity of the bulimic symptoms. There are two subscales: the symptomatology scale (30 items), that determines the seriousness of the symptoms, and the severity scale (3 items) that offers a severity index. This questionnaire has been found to have a high

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internal consistency (Cronbach's alpha coefficient range: 0.96) and has been adapted to the Spanish population (Rivas et al., 2004).

2.2.3. Symptom checklist-revised (SCL-90-R; Derogatis, 1990)

In order to evaluate a broad range of psychological problems and symptoms of psychopathology, the SCL-90-R was employed. For the present study only the global indices, namely global severity index (GSI), positive symptom distress index (PSDI) and positive symptom total (PST) were employed. This scale has been validated in a Spanish population (Derogatis, 2002), obtaining a mean internal consistency of 0.75 (coefficient alpha).

2.2.4. Social avoidance distress scale (SAD; Watson and Friend, 1969)

This 28-item scale was designed to measure the degree of distress, discomfort, anxiety and avoidance of social situations. This scale was also adapted to the Spanish population and yielded a high internal consistency (Cronbach's alpha coefficient=0.90) (Bobes et al., 1999).

2.2.5. State-trait anger expression inventory 2 (STAXI-2; Spielberger, 1996)

The STAXI-2 (Spielberger, 1996) is a 44-item self-report instrument that examines the experience and expression of anger. It entails six scales and two subscales: 1) State Anger; 2) Trait Anger (including two subscales: a) Angry Temperament and b) Reaction to criticism; 3) Anger Control (including two subscales: a.) Anger Control-Out and b.) Anger Control-In; 4) Anger Expression-In (Anger suppression); 5) Anger Expression-Out and 6) Anger Expression, which provides a general index of the expression of anger (derived from the Anger Expression-In, the Anger Expression-Out and Anger Control scales). The Spanish version of the STAXI-2 comprises 49 items and includes three additional subscales of the Anger State scale, which are a) Sentiment, b) Verbal Expression and c) Physical Expression. For the present study a summary score of these three Anger State subscales was utilized. In addition the Anger-Control scale is subdivided into a) Anger Control-In and b) Anger Control-Out. Items are rated on four-point Likert scales assessing either the intensity of the angry feelings or the frequency, with which anger is experienced, expressed, suppressed, or controlled. A higher score is always indicative of greater levels of the assessed anger construct. The STAXI-2 has been found to have good psychometric properties (including reliability and clinical validity) across a range of normal and clinical populations (Spielberger, 1996). This instrument was validated in a Spanish population with alpha Cronbach coefficients ranging between 0.63 and 0.95 (Fernández-Abascal and Martin, 1995; Miguel-Tobal et al., 1997).

2.2.6. Temperament and character inventory-revised (TCI-R; Cloninger, 1999)

The TCI-R (Cloninger, 1999) is a 240-item, five point Likert scale, reliable and valid questionnaire that measures, as in the original TCI version (Cloninger et al., 1993), seven dimensions of personality: four temperament (Harm Avoidance, Novelty Seeking, Reward Dependence and Persistence) and three character dimensions (Self-Directedness, Cooperativeness and Self-Transcendence). The performance on the Spanish version of the original questionnaire (Gutierrez et al., 2001) and the revised version have been documented (Gutiérrez-Zotes et al., 2004). The scales in the latter showed an internal consistency (coefficient alpha) of 0.87.

2.2.7. General health questionnaire-28 (GHQ-28; Goldberg, 1981)

The GHQ-28 is a self-report questionnaire that has been designed to detect and assess individuals with an enlarged probability of a present psychiatric disorder. The GHQ-28 comprises four subscales: Somatic Symptoms, Anxiety and Insomnia, Social Dysfunction, and Severe Depression. In the current study a cut off score of 6/7 (6=no case; 7=case) was employed to exclude individuals with an elevated likelihood of a present psychiatric disorder. In previous studies this cut off score has yielded a sensitivity of 76.9% and a specify of 90.2% (Lobo et al., 1986). The GHQ-28 has been studied in various European countries and has been found to be a valid and reliable tool (Goldberg and Williams, 1996).

2.2.8. Structured face to face interview (First et al., 1997)

Structured face to face interviews were used to assess self-harm, where actual or lifetime regular self-injurious behaviours were considered (cutting/ burning/ hitting/ scratching/ hair pulling), as all direct and intentional physical self-damage behaviours which did not lead to conscious death. Additionally, impulse control disorder and substance abuse/dependence, considering lifetime ICDs and alcohol and drug abuse/dependence, were assessed with the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 1997) and Lifetime suicide attempts (with the question "Have you ever attempted suicide?").

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2.3. Procedure

In addition the battery of assessments, the eating disorder group was assessed by a structured clinical interview regarding their eating disorder and psychopathological symptoms and their family history of eating disorders (Fernández-Aranda and Turon, 1998). Interviews were conducted by experienced clinical psychologists with masters or doctoral degrees in a mental-health discipline, who were not blind to diagnosis. Healthy controls were recruited from individuals visiting the hospital for routine blood tests. For the control group, screening for a current or lifetime eating disorder and/or general distress was measured by the GHQ-28 (Goldberg, 1981). None of the controls had a history of mental illness. All controls were from the same catchment areas as index patients. Demographic information was also obtained from all participants.

2.4. Statistical analysis

Analyses were carried out with SPSS 14.0. All significance tests were two-tailed and the Bonferroni correction was employed to control for multiple comparisons. Firstly, the anger expressions (STAXI-2 scores) between eating disorder patients and controls were compared. Analyses of covariance procedures were used for comparing the means obtained through the STAXI quantitative measures. For the categorical STAXI-2 variable "anger state" (null-low-moderate-high) the proportions comparison was carried out by estimating the corresponding OR after defining "null" as reference category. Since AN and BN patients differed significantly in age of onset and duration of the disorder all analyses were adjusted by these variables.

Secondly, the predictive value of the variables measuring anger expressions on the bulimic behaviors was analyzed. We defined five different criteria for the eating disorder patients: the presence of bulimic behavior (yes/no) and the weekly frequency of bingeing and vomiting episodes as well as laxative, and diuretic self-administration. Logistic regression models were used for the binary criterion "presence of bulimic symptoms" and multiple regressions for the other quantitative dependent variables. Global predictive value was estimated with Nagelkerke's R^2 (logistic regressions) and adjusted R^2 (linear regressions) coefficients. Independent models were also adjusted for the partial and total scores obtained from the STAXI-2 questionnaire. Finally, regressions were once again adjusted by age of onset and duration of the disorder.

Next, the association between the anger expressions and the primary clinical and personality features obtained

Table 1
Comparison of anger expression between eating disorder patients and controls

		Adjusted means		Means comparisons (ANCOVA)		
		ED	Controls		MD	95% CI (MD)
Trait anger/ angry temperament		61.4	31.5	<0.0005	29.8	22.8; 36.8
Trait anger/ angry reaction		56.3	27.4	<0.0005	28.9	21.8; 35.9
Trait anger		62.4	26.1	<0.0005	36.3	29.2; 43.4
Anger expression-out		53.8	35.9	<0.0005	17.9	10.5; 25.2
Anger expression-in		56.6	33.3	<0.0005	23.2	16.2; 30.2
Anger control-out		41.0	62.0	<0.0005	−21.0	−27.9; −14.1
Anger control-in		40.7	54.6	0.0036	−13.9	−21.5; −6.3
Anger expression index		64.2	32.6	<0.0005	31.6	24.6; 38.7
		Percentage		Proportions comparison (Logistics)		
		ED	Controls	P	OR	95% CI (MD)
State anger	High	3.9%	0.0%	–	–	–
	Moderate	16.3%	1.0%	0.0002	37.5	4.90 290
	Low	51.1%	33.7%	0.0009	3.46	1.95 6.15
	Null	28.8%	65.5%	*Reference level for estimating OR*		

Statistical procedures are adjusted by age of onset and illness duration and results include Bonferroni's correction.
Samples size: ED=135 and Controls=103. MD: Mean difference (ED-Controls); OR: odds ratio *vs.* null level.
– The parameter could not be estimated.

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Table 2
Logistic and linear regressions for exploring the predictive value of anger on bulimic behaviors

		Bulimic behaviors (yes/no)[a]			Frequency of vomits[b]				Frequency of laxatives[b]				Frequency of diuretics[b]				Frequency of binges[b]			
		OR	*P*	95% CI	R^2	*B*	*β*	*P*	95% CI: B	R^2	*B*	*β*	*P*	95% CI: B	R^2	*B*	*β*	*P*	95% CI: B	R^2
	Trait anger/angry temperament	1.01	0.06	1.00; 1.03	0.13	0.01	0.04	0.73	−0.04; 0.06	0.03	−0.00	−0.00	1.00	−0.05; 0.05	0.01	0.02	0.14	0.14	−0.01; 0.05	0.05	0.00	.001	0.95	−0.05; 0.05	0.03
	Trait anger/ angry reaction	0.99	0.37	0.98; 1.01		−0.03	−0.12	0.22	−0.08; 0.02		0.00	0.01	0.90	−0.05; 0.05		−0.03	−0.18	0.06	−0.06; 0.00		0.01	.047	0.63	−0.04; 0.06	
	Anger expression-out	1.01	0.45	.990; 1.02	0.13	−0.02	−0.09	0.42	−0.08; 0.03	0.03	−0.00	−0.01	0.93	−0.05; 0.05	0.05	−0.01	−0.42	0.67	−0.04; 0.03	0.04	0.00	.005	0.96	−0.05; 0.05	0.05
	Anger expression-in	1.01	0.15	1.00; 1.03		0.02	0.07	0.49	−0.03; 0.07		0.06	0.21	0.03	0.01; 0.10		0.01	0.90	0.37	−0.02; 0.05		0.02	.086	0.36	−0.03; 0.07	
	Anger control-out	1.01	0.46	1.00; 1.03		−0.04	−0.14	0.23	−0.10; 0 .03		0.04	0.01	0.90	−0.06; 0.06		−0.02	−1.2	0.24	−0.06; 0.02		0.00	.001	1.00	−0.06; 0.06	
	Anger control-in	1.00	0.71	0.99; 1.02		−0.01	−0.04	0.72	−0.06; 0.04		0.01	0.04	0.70	−0.04; 0.06		0.02	0.98	0.33	−0.02; 0.05		−0.03	−.11	0.25	−0.08; 0.02	
	Trait anger total score	1.01	0.47	0.99; 1.02	0.10	−0.05	−0.18	0.09	−0.10; 0.01	0.05	−0.02	−0.01	0.94	−0.06; 0.05	0.01	−0.01	−0.06	0.61	−0.04; 0.03	0.03	−0.01	−.06	0.60	−0.07; 0.04	0.05
	Anger expression total index	1.00	0.98	0.98; 1.02		0.06	0.21	0.06	−0.01; 0 .12		0.07	0.02	0.85	−0.05; 0.06		0.00	0.00	0.99	−0.04; 0 .04		0.05	.18	0.10	−0.01; 0.11	
	State anger Low vs. Null	1.11	0.82	0.44; 2.78	0.13	1.57	0.10	0.33	−1.60; 4.74	0.02	1.16	0.08	0.45	−1.90; 4.18	0.04	0.47	0.05	0.64	−1.50; 2.44	0.03	1.06	.071	0.49	−2.00; 4.10	0.03
	Moderate vs. Null	1.43	0.58	0.41; 5.03		1.49	0.07	0.48	−2.70; 5.66		3.62	0.19	0.07	−0.31; 7.55		−0.45	−0.04	0.73	−3.00; 2.13		1.52	.076	0.45	−2.50; 5.50	
	High vs. Null	–	–	–		2.61	0.06	0.53	−5.60 10.8		−0.69	−0.02	0.86	−8.50; 7.03		−0.27	−0.01	0.92	−5.30; 4.81		2.02	.046	0.61	−5.90; 9.90	

B:Non-standardized coefficient, *β*: Standardized coefficient.
– The parameter could not be estimated. Independent models obtained for individual and total scores. Regressions are adjusted by age of onset and illness duration.
[a] Logistic models for binary response purging (yes/no).
[b] Linear models for frequency of vomits, laxatives, diuretics and binges.

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Table 3
Correlations between anger expression and clinical and personality psychometrical measures in eating disorder patients

	Trait ang/T	Trait ang/R	Trait total	AE out	AE in	AC out	AC in	Expres.index	Anger state
EDI2: total score	0.367**	0.334**	0.429*	0.312**	0.488**	−0.211*	−0.225*	0.386**	0.295**
BITE: symptoms score	0.180*	0.065	0.156	0.170	0.284**	−0.057	−0.148	0.233**	0.159
BITE: severity score	0.194*	0.049	0.130	0.185*	0.181*	−0.147	−0.074	0.181*	0.217*
SAD score	0.294**	0.244**	0.319**	0.287**	0.354**	−0.223*	−0.174	0.260**	0.235**
SCL-90-R: GSI score	0.480**	0.337**	0.470**	0.330**	0.532**	−0.184*	−0.220*	0.387**	0.449**
SCL-90-R: PST score	0.439**	0.229**	0.386**	0.251**	0.397**	−0.169	−0.192*	0.302**	0.364**
SCL-90-R: PSDI score	0.381**	0.397**	0.466**	0.344**	0.555**	−0.147	−0.206*	0.367**	0.401**
TCI-R: Novelty seeking	0.143	0.107	0.126	0.091	−0.044	0.011	0.023	0.057	0.037
TCI-R: Harm avoidance	0.170	0.298**	0.290**	0.167	0.232**	−0.137	−0.159	0.120	0.172
TCI-R: Reward dependence	−0.163	−0.198*	−0.211*	−0.075	−0.352**	0.083	0.170	−0.107	−0.145
TCI-R: Persistence	−0.036	−0.108	−0.077	−0.094	0.053	0.069	0.088	0.027	−0.009
TCI-R: Self-directedness	−0.449**	−0.409**	−0.500**	−0.264**	−0.444**	0.135	0.343**	−0.365**	−0.362**
TCI-R: Cooperativeness	−0.338**	−0.323**	−0.361**	−0.138	−0.262**	0.112	0.202*	−0.198*	−0.277**
TCI-R: Self-trascendence	0.115	−0.065	0.036	0.031	0.141	0.054	0.076	0.042	0.152

Trait Ang/T: Trait Anger/Angry Temperament; Trait Ang/R: Trait Anger/Angry Reaction; AE Out: Anger Expression-Out; AE In: Anger Expression-In; AC Out: Anger Control-Out; AC In: Anger Control-In; Expres. Index: Total Anger Expression Index; Anger State: ordinal variable measuring Global Anger State.
EDI-2: Eating Disorder Inventory 2; BITE: Bulimic Investigatory Test Edinburgh; SAD: Social Avoidance Distress Scale; SCL-90-R: Symptom Checklist 90-Revised; GSI: Global Severity Index; PST: Positive Symptom Total; PSDI: Positive Symptom Distress Index; TCI-R: Temperament and Character Inventory-Revised.
*Significant correlation at 0.05 level; **Significant correlation at 0.01 level.

only for the eating disorder patients was estimated. Pearson's correlation coefficient was used for the STAXI-2 quantitative variables and Spearman's non-parametric coefficient for the STAXI-2 categorical-ordinal variable "anger state."

Finally, (for eating disorder patients) comorbidity between anger expressions and self-damaging impulsive behaviors was evaluated for alcohol-drug abuse, suicidal ideation-attempts, self-harm, kleptomania, and compulsive buying. These associations were evaluated through odds ratios (OR) estimated with logistic regression models adjusted by the patients' diagnostic subtype. Independent models were defined for the total and partial scores obtained through the STAXI-2.

3. Results

3.1. Anger in women with eating disorders and controls

Table 1 contains the comparisons of anger expressions between eating disorder patients and controls. These results indicate that women with eating disorders obtained higher mean scores than the controls on all the STAXI-2 scales except for the Anger Control (In–Out), where the scores were lower for the eating disorder patients. The global "Anger State" level also differed between patients and controls: only 1% of individuals without an eating disorder acquired a moderate level on this variable (0% obtained a high score), whereas 20.2% of the eating disorder patients reported moderate or high levels. The odds of achieving low *vs.* null level was 3.46 times higher for the eating disorder patients and the odds of moderate *vs.* null level was 37.5 times higher.

3.2. Anger and bulimic behaviors

Regarding the predictive value of anger expressions on bulimic behaviors, Table 2 indicates that the frequency of laxative use is increased for women with higher scores on the Anger Expression-In scores ($B=0.06$; $P=0.03$). No statistical association was found between general bulimic behaviors, weekly frequency of vomiting, bingeing and diuretic use and any of the remaining STAXI-2 scales.

3.3. Anger and clinical and personality features in eating disorders

As shown in Table 3, Anger expression was positively associated to several clinical eating disorder symptoms, measured by the EDI-2 and BITE, but also to SAD scores. Regarding personality traits (TCI-R scores), whereas Harm Avoidance was positively associated with Anger expression scales, Reward Dependence was negatively related. Conversely, Self-directedness and Cooperativeness TCI-R scores, yielded negative correlations for the STAXI-2 scales, except for the Expression Index and State Anger.

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3.4. Anger and psychopathology

As shown in Table 3, almost all the current psychopathological symptoms (measured by SCL 90-R) were positively related to Anger Expression, whereas Anger Control subscales (In–Out) were negatively correlated. Independent of diagnostic subtype, higher scores in Anger Expression-Out are linked to decreased odds of suicide attempts (OR=0.98, 95% CI: 0.96 to 0.99; P=0.011), and higher scores in Anger Control-Out are associated with decreased odds of compulsive buying (OR=0.97, 95% CI: 0.95 to 0.99; P=0.018). Moreover, higher Anger Expression-In was related to increased odds of self-harm behavior (OR=1.03, 95% CI: 1.01 to 1.04; P=0.001). Alcohol and drugs abuse, suicidal ideation and kleptomania were not statistically significantly correlated with any measures of anger expressions.

4. Discussion

The current study compared various facets of anger in individuals with eating disorders and healthy controls, explored the relation between anger and bulimic behaviors, and assessed the association between anger and eating disorder symptoms, general psychopathological features, and personality traits and explored the relation between anger and self-harm behaviors.

4.1. Anger in women with eating disorders and controls

Our first hypothesis was that eating disorder patients would exhibit higher scores on the anger expression index than controls. Correspondingly, the present results revealed that women with eating disorders obtained higher mean scores than the controls on all the STAXI-2 scales except for the Anger Control (In–Out) subscales. These results support the findings of previous studies indicating that eating disorder patients report higher anger levels than controls (Fassino et al., 2001). They suggest that eating disorder patients may have inadequate anger expression and skill deficits in dealing with anger and frustration. The extent to which this inadequate anger expression is associated with the development and maintenance of abnormal eating patterns remains unclear.

4.2. Anger and bulimic behaviors

Our second hypothesis that individuals who exhibit bulimic behaviors would exhibit significantly higher scores on the Anger Expression-In subscale than the patients without bulimic symptomatology, was supported, but only for frequency of laxative use. This finding is compatible with the results of research showing that laxative use is related to anger in general (Tozzi et al., 2006) and to anger suppression in particular (Waller et al., 2003; Truglia et al., 2006). The finding that only laxative use was directly associated with anger suppression indicates that different purging methods may be related to different facets of anger, as suggested by a previous study (Reba et al., 2006).

4.3. Anger and clinical, general psychopathology and personality features

A further objective of the present study was to assess the relation between general anger expression and eating disorder symptoms, psychopathological features, and selected personality traits. Our results suggest that anger expression was positively related to eating disorder severity. Correspondingly, previous studies have reported associations between severity of disturbed eating patterns and difficulty in expressing anger (Fava et al., 1995). Another emergent finding was that general psychopathology and social anxiety were also positively linked to anger expression. Interestingly, compulsive buying was found to be negatively associated with Anger Control-Out. As reported in previous studies, compulsive buying is one of the most frequently prevalent impulse control disorders in eating disorders (Fernández-Aranda et al., 2006), and the most common chronology of onset pattern was for compulsive buying to precede eating disorders (Fernandez-Aranda et al., in press). This observation lends itself to the interpretation that a lack of Anger Control-Out, mediated by specific adverse environmental exposures and genetic factors, may predispose to some specific impulse control disorders, namely compulsive buying. Summarizing, eating disorders patients with abnormal anger expression seem to present higher eating disorders severity and more general psychopathology.

Finally in relation to personality, various significant relationships were found between the general anger expression and some personality traits, namely harm avoidance and reward dependence. This finding contradicts previous studies that have indicated no association between personality, disordered eating and different ways of managing aggressive feelings in eating disordered individuals (Fassino et al., 2001). As expected, Harm Avoidance, commonly found in individuals with eating disorders (Fassino et al., 2003a; Klump et al., 2004), was positively related to Trait Anger-Angry Reaction and Anger Expression-In. Contrastingly, Reward Dependence was found to be

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negatively related to Trait Anger-Angry Reaction and Anger Expression-In. This seems logical as individuals who rely on others for approval and reward are unlikely to view outwardly directed anger to be in service of those interpersonal goals.

4.4. Anger and self-harm behaviors

Our final hypothesis was that individuals with an intense urge to express anger would also display a variety of impulsive self-harm behaviors. In fact, in our sample, patients with higher Anger Expression-In and lower Anger Expression-Out were more likely to present associated self-harming (e.g. cutting, burning, suicide attempts) behaviors. A variety of self-destructive behaviors have been described in eating disorder patients (Claes et al., 2005; Solano et al., 2005). One possible interpretation is that individuals with eating disorders who internalize anger and have skill deficits in expressing anger may be more likely to engage in self-harm behaviors.

4.5. Treatment implications

The results of the present study also have clinical implications. First, the results emphasize the importance of conceptualizing anger as a multifaceted phenomenon. Second, bulimic behaviors were related to trait anger and thus reflect a more stable predisposition toward anger than previously thought. This indicates that anger is not just merely caused by the presence of eating disorders and that it is therefore essential to address it primarily. Therefore, if replicated, these findings support the further evaluation of the efficacy of affect-oriented treatments (e.g. dialectical behavior therapy) in eating disorders which target anger and hostility with the goal of improving the adaptive management of these emotions. This could be achieved by substituting emotion-focused coping mechanisms with a more problem-focused technique. The presence of certain bulimic behaviors such as laxative abuse might indicate which facets of anger need to be addressed therapeutically (Telch, 1997; Evershed et al., 2003; Palmer et al., 2003; Simpson et al., 2004).

4.6. Limitations

These results should be considered within the context of several limitations. First, the retrospective and self-report data collection procedures may limit the validity and the reliability of our findings, which are subject to unreliability of individual recall and potential memory bias. Second, the cross-sectional design does not allow us to determine causality of the variables assessed. Third, since we did not account for a lifetime eating disorder in the control sample, we cannot rule out that some controls may have had eating disorder symptoms. On the other hand, this represents a more realistic and natural control group and a conservative bias. Moreover, the risk of spurious results due to comorbidity of index patients with Axis I and Axis II diagnoses should be considered. Finally, given that the study did not show causal relationships, other explanations could also have accounted for our results. Future research could expand these results employing longitudinal designs addressing the potential mediating role of anger in the etiological factors and clinical course of eating disorders.

In conclusion, this study found that among eating disorder patients anger is a common problem that merits further exploration. Furthermore, this study showed that diverse bulimic behaviors are related to different anger expressions. The present findings also contribute to an improved understanding of how the different facets of anger are associated to eating disorders symptomatology, clinical general psychopathological features, and personality traits. Finally, we observed that inappropriate anger expression was associated with self-harm behaviors in this population.

5. Uncited reference

Cloninger, 1987

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8.8. Study 8

Comparison study of full and subthreshold bulimia nervosa: Personality, clinical characteristics, and short-term response to therapy

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INTRODUCTION

Even though there is a body of evidence on the efficacy of CBT for threshold BN, strikingly little is known about the treatment and course of sub-BN diagnoses. This omission of treatment response of sub-BN patients is critical for several reasons. First, research has documented the clinical significance of subthreshold eating-related problems that have evolved from previous eating disorders (Lewinsohn, Striegel- Moore, & Seeley, 2000). Second, there is evidence that the severity of psychopathology and degree of secondary psychosocial impairment in those with sub-BN are comparable to those seen in patients with anorexia nervosa (AN) or BN (Ricca et al., 2001; Turner & Bryant-Waugh, 2004).

OBJECTIVES

In the context of a brief outpatient psychoeducational intervention for BN and sub-BN, the goals of the current study are twofold:

(a) to report symptomatological and personality differences between threshold and sub-BN cases.

(b) to compare the short-term response to a brief outpatient psychoeducational intervention in individuals with full and sub-BN.

HYPOTHESES

We hypothesized that, even though full-BN and sub-BN patients would diverge on baseline ED symptomatology, they would both profit from a brief psychoeducational intervention.

METHOD

PARTICIPANTS

78 BN patients (39 full vs. 39 partially diagnosed-EDNOS) admitted to our Unit participated in the study. All patients were female. In both groups, the same brief-outpatient psycho-educational therapy was applied (6 sessions of 90 minutes).

ASSESSMENT

The following tests were administered before and after the intervention:

- The Eating Attitude Test (EAT-40)
- The Eating Disorder Inventory 2 (EDI-2)
- The Symptom Checklist-Revised (SCL-90-R)
- The Bulimic Investigatory Test Edinburgh (BITE)
- The Temperament and Character Inventory-Revised (TCI-R)
- The Social Avoidance Distress Scale (SAD)
- Other clinical and psychopathological indices

RESULTS

- With exception of higher depression (p=0.29) and phobic anxiety (p=0.45) in full-BN, there were no significant differences on any other scales of general psychopathology or personality traits between the two groups.
- At the end of treatment, there were no significant differences between groups on the following:
- - abstinence rates for binge eating and vomiting (33.3% full-BN vs. 35.2% sub-BN, p=0.461)
- - number of sessions attended (adjusted mean: full-BN=5.4 vs. sub-BN=4.6; p=0.084)
- - drop-out rates (OR=0.94; p=0.960).

DISCUSSION

Threshold and subthreshold BN share common psychopathological symptoms and personality traits.

No differences in therapy outcome were observed for the two groups after a brief group psychoeducational intervention.

Figure 1: Psychoeducational Program

Table 1 Clinical and psychological features at the beginning

Quantitative measures	Mean (SD) BN (N=78)	Sub-BN (N=39)	Mean comparisons t	p	95% CI (MD)
TCI-R: Novelty seeking	108.1 (15.7)	107.8 (14.9)	.071	0.940	-4.89 7.33
TCI-R: Harm avoidance	116.7 (24.9)	113.9 (19.4)	.548	0.587	-7.44, 13.08
TCI-R: Reward dependence	104.5 (16.6)	105.3 (15.6)	.209	0.721	-6.83, 5.88
TCI-R: Persistence	106.2 (16.7)	112.6 (17.1)	1.63	0.106	-14.2, 1.44
TCI-R: Self-directedness	116.3 (23.3)	117.8 (23.6)	.272	0.626	-13.2, 8.11
TCI-R: Cooperativeness	136.7 (17.7)	133.5 (13.6)	.891	0.376	-4.94, 16.16
TCI-R: Self-transcendence	68.3 (15.2)	69.7 (15.9)	.381	0.697	-6.39, 5.58

Categorical measures	Percentage - % (95% CI) BN (N=78)	Sub-BN (N=39)	Percentages comparisons χ^2	p	95% CI (RR)
Alcohol abuse	10.3 (2.67, 24.2)	8.7 (1.71, 22.5)	.082	.999	0.39, 5.13
Other drugs abuse	17.9 (7.54, 33.5)	11.1 (3.11,26.1)	.999	.403	0.52, 5.06
Self-harm behavior	30.8 (17.5, 47.9)	31.4 (16.9,49.3)	.004	.951	0.58, 1.93
Suicidal ideation	43.6 (27.8, 60.4)	41.7 (25.5,59.3)	.029	.866	0.60, 1.71
Suicidal attempts	30.8 (17.5, 47.9)	22.2 (10.1,39.2)	.999	.403	0.84, 3.99
Hyperactivity (medium-high)	60.5 (43.4, 76.0)	47.1 (29.8,64.5)	1.51	.252	0.83, 2.90
Obesity in childhood	7.7 (1.61, 20.9)	8.6 (1.80, 23.1)	.019	.999	0.19, 4.16
Neurosis in family history	23.7 (11.4, 40.2)	8.6 (1.80, 23.1)	3.63	.082	0.91, 9.39
Distress in family history	15.4 (5.88, 30.5)	28.6 (8.44,36.3)	.271	.602	0.29, 2.37
Obesity in family history	17.9 (7.53, 33.5)	22.9 (10.4,40.1)	.270	.609	0.32, 1.54
Alcohol abuse in family history	23.1 (11.1, 39.3)	28.6 (14.6,46.3)	.252	.589	0.37, 1.76
Affective dis. in family history	47.5 (44.8, 78.9)	66.6 (42.1,76.1)	.518	.800	0.71, 1.48

MD: mean difference; PR: proportion ratio; CI: confidence interval.
TCI-R: Temperament and Character Inventory-Revised.

Table 2. Study of the changes betw-een pre and post treatment.

	Pre and post mean clinical data: Initial mean BN (N=39)	Initial mean Sub-BN (N=39)	Final mean BN (N=34)	Final mean Sub-BN (N=29)	Comparison of adjusted mean changes: Mean changes BN	Mean changes Sub-BN	ANCOVA results: MD	p	95% CI (MD)
Weekly freq. of binges	8.9 (5.6)	7.2 (3.5)	1.1 (1.2)	2.6 (3.7)	-8.4	-.66	-5.54	< .0005	-7.54; -3.54
Weekly freq. of vomits	7.5 (6.5)	2.6 (4.6)	1.9 (1.7)	2.4 (4.9)	-5.9	-2.06	-3.86	.001	-5.82; -1.89
Weekly freq. of laxatives	6.4 (10)	1.4 (4.6)	2.5 (8.5)	.46 (1.7)	-6.5	-2.52	-4.26	.001	-6.49; -1.91
Weekly freq. of diuretics	1.6 (2.5)	1.5 (3.4)	.77 (2.5)	.11 (.58)	-.91	-.91	.596	.747	-2.12; 2.92
Body mass index (BMI)	23.9 (2.8)	21.9 (2.4)	23.2 (2.4)	22.6 (2.4)	.64	.14	-.896	.532	-.436; .242
EAT: total score	53.5 (19.8)	47.3 (24.4)	35.3 (23.3)	35.5 (23.6)	-18.8	-12.1	-7.68	.270	-21.5; 5.53
EDI-II: total score	112 (47.2)	96.5 (48.4)	84.7 (46.8)	73.1 (49.2)	-29.4	-29.9	-3.58	.821	-37.5; 26.9
BITE: symptoms scale	24.6 (4.1)	21.3 (5.7)	20.6 (7.4)	19.3 (7.4)	-4.54	-2.8	-1.71	.552	-7.63; 4.23
BITE: severity scale	13.8 (7.5)	10.8 (7.5)	8.6 (7.1)	8.5 (8.4)	-6.63	-2.2	-3.93	.121	-8.91; 1.05
SAD: total score	13.6 (6.4)	10.5 (7.3)	10.8 (6.7)	12.2 (8.8)	-.46	2.8	3.33	.394	-3.43; 9.09
SCL-90-R: GSI	1.81 (0.8)	1.49 (0.7)	1.4 (0.8)	1.2 (1.0)	-.39	-.36	.074	.768	-.442; .589
SCL-90-R: PSDI	2.33 (0.8)	2.12 (0.8)	2.0 (.89)	1.8 (.73)	-.23	-.27	.044	.856	-.460; .549
SCL-90-R: PST	68.5 (18.9)	69.8 (18.7)	58.7 (25.7)	59.6 (24.6)	-7.87	-10.8	2.33	.760	-13.7; 18.4

*Results adjusted by frequency of binge eating and purging at baseline. Change differences post-pre values.
MD: mean difference; CI: confidence interval; BMI: body-mass index (kilos/ kgm²).
EAT: Eating Attitudes Test; EDI-II: Eating Disorders Inventory; BITE: Bulimic Investigatory Test Edinburgh;
SAD: Social Avoidance Distress Scale; SCL-90-R: Symptom Checklist- Revised.

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Comparison study of full and subthreshold bulimia nervosa: Personality, clinical characteristics, and short-term response to therapy

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Abstract
This study compared symptomatological and personality differences between individuals with threshold bulimia nervosa (BN; $n = 39$) and those with subthreshold BN ($n = 39$) and their short-term response to a brief outpatient intervention. Participants were matched using a pairwise matching procedure, taking into account age, age of onset, and duration of the disorder. Both groups received the same brief outpatient psychoeducational therapy. The same assessment measures were used before and after treatment. With the exception of some clinical and psychopathological symptoms (higher depression and phobic anxiety in threshold BN), there were no significant between-group differences on scales of general psychopathology or personality traits. At the end of treatment, there were no significant between-group differences on abstinence rates for binge eating and vomiting, number of sessions attended, or dropout rates. Threshold BN and subthreshold BN share common psychopathological symptoms and personality traits. No differences in therapy outcome were observed for the two groups after a brief group psychoeducational intervention.

The point prevalence of threshold bulimia nervosa (BN) has been estimated to be between 3% and 7% in young female general practice attendees and from 0.5% to 1.0% in community samples (Bushnell, Wells, Hornblow, Oakley-Browne, & Joyce, 1990; Hoek & van Hoeken, 2003). Despite the prevalence and associated medical and psychiatric morbidity, only a small proportion of individuals with BN seek treatment (Arnow, 1999; Hudson, Hiripi, Pope, & Kessler, 2006). This mismatch between prevalence and treatment seeking may be due in part to difficulties in finding specialized treatment settings for BN and the high costs and logistics associated with face-to-face individual psychotherapy (King, 1989).

Threshold Versus Subthreshold BN Cases

Subthreshold BN (sub-BN) is more common than full, threshold, BN (Hoek, 1993; Wade, Bergin, Tiggemann, Bulik, & Fairburn, 2006). People with sub-BN generally exhibit eating disorders of clinical severity but do not meet criteria for full BN. Technically, individuals with sub-BN are considered to have eating disorder not otherwise specified (EDNOS) (American Psychiatric Association [APA], 2000a). Although EDNOS is a residual diagnostic category, strikingly, the majority of individuals seeking treatment for an eating disorder (25–60%) fall into this category (Anderson, Bowers, & Watson, 2001; Grilo, Devlin, Cachelin, & Yanovski, 1997; Rodriguez-Cano, Beato-Fernández, & Belmonte-Llario, 2005). Arguments exist for removing sub-BN from the EDNOS category and placing it under the BN diagnostic heading. This could be accomplished either by relaxing the diagnostic criteria for BN or by introducing a severity index (Fairburn & Bohn, 2005). Further research is needed to determine the optimal approach to classification and subclassification of

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eating disorders. The present study contributes to this literature by exploring differences in response to a brief group psychoeducation intervention in individuals with threshold and sub-BN.

Personality Differences between Threshold and Subthreshold Bulimia Nervosa

An important dimension to consider when studying outcome in eating disorders is underlying personality traits (Wagner et al., 2006). Bulimic patients are generally characterized by high impulsivity, sensation seeking, and novelty seeking (Fernández-Aranda et al., 2006). It remains unclear whether differences in these traits between patients with BN and recovered individuals are factors that add to an unfavorable outcome or are a result of malnutrition augmenting the symptoms (Klump et al., 2004). Research on this topic has yielded contradictory findings. Some studies indicate that a wide range of common eating disorder symptoms continue after recovery and do not differ between eating disorder subtypes, suggesting that they are traits rather than state-related disturbances. (Klump et al., 2004; Wagner et al., 2006). Other studies have shown that recovery from eating disorders may have an attenuating influence on the symptoms of personality disorders (Marino & Zanarini, 2001; Matsunaga et al., 2000). Additional focused research is, therefore, required to clarify these inconsistencies.

Efficacy of Face-to-Face Individual Psychotherapy for Full and Subthreshold Bulimia Nervosa

Causal and maintenance factors of BN have been conceptualized from several theoretical perspectives. Cognitive–behavioral therapy (CBT), based on the cognitive model postulated by Fairburn et al. (Fairburn, 1997; Fairburn, Marcus, & Wilson, 1993a), is considered to be the psychotherapeutic treatment of choice supported by its good outcomes in randomized controlled trials (Agras, Walsh, Fairburn, Wilson, & Kraemer, 2000). CBT has proven superior to no treatment (Fairburn, Agras, & Wilson, 1992), to antidepressant treatment (Agras et al., 1992), and to other forms of psychotherapy, including supportive–expressive therapy (Garner et al., 1993), psychodynamic therapy (Walsh et al., 1997), and short-term focal psychotherapy (Fairburn, Kirk, O'Connor, & Cooper, 1986). Only interpersonal psychotherapy (IPT) has demonstrated similar outcomes to CBT, although the course of recovery with IPT is more protracted (Agras, Crow, et al., 2000).

Efficacy of Brief Group Psychoeducation or other Brief or Non-Therapist-Led Approaches

Face-to-face individual psychotherapy is logistically complicated, requires considerable therapist training, and is often difficult to find outside of regions that contain specialized treatment settings. For BN, the efficacy of various forms of psychoeducational approaches that do not require the same intensity of intervention, measured by abstinence rates from binge eating and purging, varies in the literature between 20% and 35% (Davis, Olmsted, & Rockert, 1990; Fernández-Aranda et al., 1998, 2004). Although these abstinence rates are not as consistently high as those observed in individual face-to-face therapy trials (Fairburn, Jones, Peveler, Hope, & O'Conner, 1993; Fairburn, Marcus, & Wilson, 1993), given the potential broader public health reach of these interventions, these numbers are promising. In general, these interventions are particularly suited to patients who demonstrate less severity and psychopathology (Davis, Olmsted, Rockert, Marques, & Dolhanty, 1997; Fernández-Aranda et al., 2004). To date, no studies have explored the applicability of these approaches across a spectrum of severity in individuals with BN.

In terms of treatment response of individuals with sub-BN, virtually nothing is known because there have been no studies of the treatment of these patients. Exceptions are two studies conducted by Nevonen et al. (Nevonen & Broberg, 2006; Nevonen, Broberg, Lindstroem, & Levin, 1999) that tested a CBT group psychotherapy model immediately followed by IPT for both full-BN and sub-BN patients. Findings revealed significant pre-to posttreatment differences for eating disorder symptoms and attitudes as well as interpersonal problems and general psychopathology for both BN groups, which could even be observed at 1- and 2.5-year follow-ups.

This omission of treatment response of sub-BN patients is critical for several reasons. First, research has documented the clinical significance of subthreshold eating-related problems that have evolved from previous eating disorders (Lewinsohn, Striegel-Moore, & Seeley, 2000). Second, there is evidence that the severity of psychopathology and degree of secondary psychosocial impairment in those with sub-BN are comparable to those seen in patients with anorexia nervosa (AN) or BN (Ricca et al., 2001; Turner & Bryant-Waugh, 2004).

In summary, even though there is a body of evidence on the efficacy of CBT for threshold BN, strikingly little is known about the treatment and course of sub-BN diagnoses.

Aims of the Study

In the context of a brief outpatient psychoeducational intervention for BN and sub-BN, the goals of the current study are twofold: (a) to report symptomatological and personality differences between threshold and sub-BN cases and (b) to compare the short-term response to a brief outpatient psychoeducational intervention in individuals with full and sub-BN. We hypothesized that, even though full-BN and sub-BN patients would diverge on baseline eating disorder symptomatology, they would both profit from a brief psychoeducational intervention.

Method

Participants

Entry into the study was between January 2004 and January 2005. The total sample included 78 female patients who were admitted for treatment at the Eating Disorders Unit of the Department of Psychiatry at the University Hospital of Bellvitge. Thirty-nine women fulfilled the *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition, text revision [*DSM–IV–TR*]; APA, 2000a) criteria for threshold BN (full-BN group), and 39 were diagnosed with sub-BN. The latter diagnosis was given if the individual met all criteria for BN but reported no objective binge episodes and no purging behavior or could not meet the frequency criteria. Given that the patients at our unit normally undergo three to four initial interviews before starting treatment, we were able to ensure that the subthreshold symptoms had been present for a minimum of 4 weeks before starting treatment. Of note, 69% of individuals with sub-BN reported having met criteria for full BN in the past. Interestingly, of these patients, 11.8% had presented a complete remission from BN, defined as being asymptomatic for at least 3 months before relapsing into the partial BN diagnosis. In the sub-BN group, 45.5% did not report an objective binge-eating episode and 21.6% did not exhibit any purging behaviors.

A pairwise matching comparison procedure was used to compose the control sample (full-BN patients); the SPSS 13 program was used so that the symptomatological and personality differences between full and sub-BN cases could be compared in a more systematic form. Each participant in the sub-BN group ($n = 39$) was paired with a randomly selected threshold BN patient of the same age, age at onset, and duration of the disorder from a larger pool of 175 full-BN individuals using propensity scores. If these procedures had not been carried out, it could have been argued that differences in treatment outcome were influenced by these variables and, therefore, did not reflect the real treatment effectiveness. Most patients were single (80.8%) and had at least some university education (71.4%). Forty-six percent of the patients were employed, and 48.7% attended consultation voluntarily. The mean age for the total sample was 23.8 years ($SD = 4.8$). There were no statistically significant differences between the two groups in age or education ($ps = .833$ and .245, respectively).

The inclusion criteria for the study were (a) female sex, (b) age greater than 18 years, (c) meeting *DSM–IV–TR* criteria (APA, 2000a) for BN or sub-BN, and (d) body mass index (BMI) greater than 18. Conversely, patients were excluded if they met any of the following criteria: (a) male sex, (b) missing values for any diagnostic items, (c) high severity of eating disorder or psychopathology, (d) current alcohol or drug abuse, or (e) current psychotic disorder. For the present analysis, the following individuals had to be excluded: (a) males ($n = 7$), because the number of males with these diagnoses was too small for meaningful comparisons, and (b) participants with greater severity of eating disorder or other psychiatric symptoms indicating inpatient intervention ($n = 36$) or individual therapeutic or medical intervention ($n = 24$). All of the patients who had been excluded from the study were treated separately with different therapeutical modalities. Disposition decisions were made by psychologists or psychiatrists who completed the anamnesis together with the treatment team according to published treatment guidelines (APA, 2000b) for CBT treatment. The Ethics Committee of our institution approved this study, and informed consent was obtained from all participants.

Measures

Eating Attitudes Test (EAT-40; Garner & Garfinkel, 1979). This questionnaire contains 40 items, including symptoms and behaviors common to eating-disordered patients, and provides an index of the severity of the disorder. Scores range from 0 to 120. The higher the score, the more disturbed the eating behavior. The cutoff score is generally set at 30 and differentiates between pathological and nonpathological populations. This questionnaire was adapted to the Spanish population, showing high internal consistency (Cronbach's $\alpha = .93$; Castro, Toro, Salamero, & Guimerá, 1991).

Eating Disorders Inventory-2 (EDI-2; Garner, 1998a). This reliable and valid 91-item multidimensional self-report questionnaire assesses different cognitive and behavioral characteristics that are

typical for eating disorders. The EDI-2 retains the 64 items (grouped into eight scales: Drive for Thinness, Bulimia, Body Dissatisfaction, Ineffectiveness, Perfectionism, Interpersonal Distrust, Interoceptive Awareness, Maturity Fears) of the EDI and adds 27 new items into three provisional scales: Asceticism, Impulse Regulation, and Social Insecurity. All of these scales are answered on a 6-point Likert scale and provide standardized subscale scores. This instrument was validated in a Spanish population (Garner, 1998b), with a mean internal consistency of .63 (coefficient alpha).

Symptom Checklist-90-Revised (SCL-90-R; Derogatis, 1990). To evaluate a broad range of psychological problems and symptoms of psychopathology, the SCL-90-R was used. This test contains 90 items and helps to measure nine primary symptom dimensions: Somatization, Obsession–Compulsion, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism. In addition, it includes three global indices: a global severity index (GSI), designed to measure overall psychological distress; a positive symptom distress index (PSDI), designed to measure the intensity of symptoms; and a positive symptom total (PST), which are reports of self-reported symptoms. The GSI can be used as a summary of the test. This scale has been validated in a Spanish population (Derogatis, 2002), obtaining a mean internal consistency of .75 (coefficient alpha).

Bulimic Investigatory Test, Edinburgh (BITE; Henderson & Freeman, 1987). This questionnaire contains 33 items that measure the presence and severity of the bulimic symptoms. There are two subscales: the Symptomatology scale (30 items), which determines the seriousness of the symptoms, and the Severity scale (three items), which offers a severity index. The cutoff point for the Symptomatology scale scores for the present study were as follows: ≤ 10 = no symptomatology, 10–20 = subclinical symptoms, and ≥ 20 clinical symptoms. The higher the score, the greater the severity. This questionnaire has been found to have an adequate internal consistency for both subscales (for Symptomatology and Severity subscales, Cronbach's $\alpha = .82$ and .63, respectively) and has been adapted to the Spanish population (Rivas, Bernabé, & Jiménez, 2004).

Temperament and Character Inventory-Revised (TCI-R; Cloninger, 1989). This reliable and valid 240-item, 5-point Likert-type questionnaire measures, as in the original TCI version (Cloninger, Svrakic, & Przybeck, 1993), seven dimensions of personality: four temperament dimensions (Harm Avoidance, Novelty Seeking, Reward Dependence, and Persistence) and three character dimensions (Self-Directedness, Cooperativeness, and Self-Transcendence). The performance on the Spanish version of the original questionnaire (Gutierrez et al., 2001) and the revised version (Gutierrez-Zotes et al., 2004) have been documented. The revised version has exhibited high internal consistency (for the different subscales, $\alpha = .77$–$.87$; Gutierrez-Zotes et al., 2004).

Social Avoidance Distress Scale (SAD; Watson & Friend, 1969). This 28-item scale was designed to measure the degree of distress, discomfort, anxiety, and avoidance of social situations. Higher scores indicate greater social avoidance and distress. A Spanish version of the present scale was applied in a clinical population (Bobes et al., 1999) and showed a cutoff point of 19. This scale was also adapted to the Spanish population and yielded a high internal consistency (Cronbach's alpha coefficient = .90).

Evaluation of sociodemographic and clinical variables. Additional demographic information, including age, martial status, education, occupation, living arrangements, motivation to receive treatment, and parental occupation, and clinical relevant variables regarding their eating disorder and psychopathological symptoms and family history of eating disorders were assessed by a structured clinical interview (Fernández-Aranda & Turon, 1998).

Procedure

Experienced psychologists and psychiatrists with master's or doctoral degrees conducted a 2-hr structured diagnostic face-to-face interview with participants to measure eating disorder symptoms and psychopathological traits. Eating disorder diagnoses were based on this interview and were consensually derived among members of the clinical team who had participated in the assessment. In addition to a comprehensive clinical and psychological evaluation (including the instruments mentioned previously), further demographic information was obtained. Finally, participants completed the questionnaires individually in a room before starting the treatment. An information sheet presented at the start of the questionnaire informed the participants about the purpose of the study and ensured confidentiality of results. Furthermore, it was emphasized that participation in the study was completely voluntary and that participants were free to withdraw from the study at any time. The therapeutic approach was explained during the first

session, and therapeutic material was provided. The assessment was repeated at the end of the treatment. Remission was defined as abstinence from bingeing and purging for a minimum of 2 weeks. Previous research has generally indicated remission at 8 (Herzog et al., 1999) and 4 (Agras, Walsh, et al., 2000) weeks. Only some have referred to a 2-week period (Pyle et al., 1990). For the present study, a 2-week remission period was chosen because of the relatively short duration and intensity (6 weeks) of the psychoeducational group therapy.

Treatment

The psychoeducational brief group therapy was based on the Davis et al. (1990) model. In our study, this intervention consisted of six weekly outpatient sessions (90 min each) with a total of eight to 10 patients per group. Both full-BN and sub-BN patients were treated together in this same brief outpatient psychoeducational therapy. The range of the number of previous treatments was between zero and three. The psychoeducational group was directed by a psychologist and a cotherapist. The main objective of this brief group intervention was to offer information and psychoeducation about BN without going into details of the patients' individual problems. The topics addressed included general information and negative consequences of BN, nutritional patterns and monitoring of meal plans, preventing strategies for decreasing bingeing and purging behavior, cognitive model for the comprehension of BN, problem-solving strategies, and relapse prevention. This program and accompanying program material have already been manualized and published in Spanish (Fernández-Aranda & Turon, 1998).

Statistical Analysis

Analyses were conducted using SPSS-13. First, the differences between full- and sub-BN patients in baseline clinical and psychological features were evaluated. For quantitative responses, means were compared with Student's t tests for independent samples. For categorical responses, proportions were compared with standard Pearson's chi-square test (exact Monte Carlo procedures were used for small samples). Association measures in contingency tables (proportion ratios) were obtained with SPSS macros (Doménech, Bonillo, & Granero, 2000).

Second, because we assessed a variety of outcome variables in this study, we structured our analyses according to primary (reduction of and abstinence from bingeing and purging behaviors) and secondary (psychological, personality, comorbid psychopathology, and treatment adherence) outcome variables. Given that multiple variables are required to capture symptomatic outcome from BN (reduction of and abstinence from binge eating and purging), we considered them as a family of primary outcome variables. The statistical analyses consisted of evaluating the observed changes (after the intervention) in these clinical outcome variables. This change was measured as the difference between pre- and posttreatment responses. Next, the mean differences obtained for the full-BN and sub-BN patients were compared. Another primary outcome variable that we compared between both diagnosis subtypes was the psychological state of patients after therapy (valued as the absence of bingeing and vomiting episodes).

Finally, treatment adherence (number of sessions attended and dropout rates), a secondary outcome variable, was also compared between full-BN and sub-BN individuals at the end of the intervention. The mean changes achieved in quantitative clinical outcome measures were statistically compared between diagnosis subtypes with analyses of variance procedures adjusted by the frequency of binge eating and purging at the beginning of treatment (analysis of covariance). Binary clinical outcome measures were compared between full-BN and sub-BN patients with logistic regression models, also adjusted by frequency of binge eating and purging before the treatment.

Results

Comparison of Baseline Clinical and Personality Features

There were no significant differences between the groups on means for age (full BN = 23.9 vs. sub-BN = 23.7; $p = .83$), age of onset (full BN = 18.3 vs. sub-BN = 17.4; $p = .37$), duration of disorder (full BN = 5.8 vs. sub-BN = 6.3; $p = .65$), number of previous treatments (full BN = 0.4 vs. sub-BN = 0.7; $p = .07$), or BMI (full BN = 22.9 vs. sub-BN = 21.9; $p = .10$). However, as expected, there were significant differences on the weekly frequency of binge eating (full BN = 6.9 vs. sub-BN = 1.2; $p < .0005$) and vomiting (full BN = 7.5 vs. sub-BN = 2.9; $p = .003$) episodes. Given these considerable baseline differences, the frequency of binge eating and purging at baseline was entered as an adjustment variable into the statistical models evaluating treatment outcome.

As shown in Table I, at baseline there were no significant differences on TCI-R temperament or character dimensions between the two groups. There were no differences in total mean scores for

Table I. Clinical and Psychological Features at the Beginning.

	BN ($n=39$)		Sub-BN ($n=39$)		Means comparison			
Quantitative measure	*M*	*SD*	*M*	*SD*	*t*	*p*	95%CI	*MD*
TCI-R Novelty Seeking	108.1	15.7	107.9	14.9	.075	0.940	−6.80	7.33
TCI-R Harm Avoidance	116.7	24.9	113.9	19.4	.546	0.587	−7.44	13.06
TCI-R Reward Dependence	104.0	16.0	105.3	15.8	.358	0.721	−8.63	6.00
TCI-R Persistence	106.2	16.7	112.6	17.3	1.63	0.108	−14.2	1.44
TCI-R Self-Directedness	115.3	23.3	117.8	22.6	.475	0.636	−13.2	8.11
TCI-R Cooperativeness	136.7	17.7	133.5	13.6	.891	0.376	−4.04	10.55
TCI-R Self-Transcendence	68.3	15.2	69.7	15.0	.391	0.697	−8.30	5.58

			Percentages comparison			
Categorical measure	Percentage –% (95%CI)	Percentage –% (95%CI)	χ^2	*p*	95%CI	PR
Alcohol abuse	10.3 (2.87; 24.2)	8.3 (1.75; 22.5)	0.082	.999	0.30	5.13
Other drugs abuse	17.9 (7.54; 33.5)	11.1 (3.11; 26.1)	0.699	.403	0.52	5.06
Self-harm behavior	30.8 (17.0; 47.6)	31.4 (16.9; 49.3)	0.004	.951	0.50	1.93
Suicidal ideation	43.6 (27.8; 60.4)	41.7 (25.5; 59.2)	0.028	.866	0.62	1.77
Suicidal attempts	30.8 (17.0; 47.6)	22.2 (10.1; 39.2)	0.699	.403	0.64	2.99
Hyperactivity (medium–high)	60.5 (43.4; 76.0)	47.1 (29.8; 64.9)	1.310	.252	0.83	2.00
Obesity in childhood	7.7 (1.61; 20.9)	8.6 (1.80; 23.1)	0.019	.999	0.19	4.16
Family history						
Anorexia	23.7 (11.4; 40.2)	8.6 (1.80; 23.1)	3.003	.082	0.81	9.39
Bulimia	15.4 (5.86; 30.5)	20.0 (8.44; 36.9)	0.271	.602	0.29	2.07
Obesity	17.9 (7.53; 33.5)	22.9 (10.4; 40.1)	0.275	.600	0.32	1.94
Alcohol abuse	23.1 (11.1; 39.3)	28.6 (14.6; 46.3)	0.292	.589	0.37	1.76
Affective disorder	61.5 (44.6; 76.6)	60.0 (42.1; 76.1)	0.018	.892	0.71	1.48

Note. BN = bulimia nervosa; C = confidence interval; MD = mean difference; TCI-R = Temperament and Character Inventory-Revised; PR = proportion ratio.

SCL-90-R GSI (full BN = 1.81 vs. sub-BN = 1.49; $p = .078$), SCL-90-R PSDI (full BN = 2.33 vs. sub-BN = 2.12; $p = .131$), SCL-90-R PST (full BN = 66.5 vs. sub-BN = 60.9; $p = .195$), EDI-2 total (full BN = 113.4 vs. sub-BN = 96.5; $p = .098$), EAT (full BN = 53.5 vs. sub-BN = 47.2; $p = .228$), and SAD (full BN = 13.6 vs. sub-BN = 13.5; $p = .943$). However, full-BN women scored higher on the BITE Symptomatology (full BN = 24.8 vs. sub-BN = 21.3; $p = .002$) and Severity (full BN = 15.9 vs. sub-BN = 10.8; $p = .003$) scales (Table II). These patients also obtained higher scores on the Bulimia subscale of the EDI-2 (full BN = 10.3 vs. sub-BN = 5.62; $p = .001$) and the Depression (full BN = 2.23 vs. sub-BN = 1.80; $p = .029$) and Phobic Anxiety (full BN = 1.36 vs. sub-BN = 0.87; $p = .045$) subscales of the SCL-90-R.

Finally, the categorical clinical features measured before treatment revealed no significant differences between full- and sub-BN patients on alcohol abuse, drug abuse, self-harm behavior, suicidal ideation, suicidal attempt, hyperactivity levels, obesity during childhood, and family antecedents in any of the following variables: anorexia, bulimia, obesity, alcohol abuse, and affective disorders.

Comparison of Therapy Outcome for Full- Versus Sub-BN

Primary outcome variables: reduction of and abstinence from bingeing and purging behaviors. After controlling for baseline values, individuals with full BN reported a greater change in the frequency of weekly binge eating and vomiting episodes. Women with full BN reported a mean weekly reduction of 6.4 binges, whereas sub-BN patients reported a mean weekly reduction of 0.9 bingeing episodes ($p < .0005$). The mean reduction of vomiting episodes reported was 5.9 in patients with full BN and 2.06 in patients with sub-BN ($p = .001$). At the end of treatment, abstinence rates did not differ between the two groups (abstinence from binge eating and vomiting: full BN = 33.3% vs. sub-BN = 35.2%; $p = .461$; abstinence from binge eating: full BN = 33.3% vs. sub-BN = 39.8%; $p = .207$; and abstinence from vomiting: full BN = 57.3% vs. sub-BN = 62.5%; $p = .752$). Weekly frequency of laxative use also showed a greater decrease in full-BN patients ($p = .001$) compared with sub-BN patients. (See Table II for a between-group comparison of changes, measured as the pre–post change scores.)

Table II. Study of the Changes Between Pre- and Posttreatment.

	Clinical state (*M*)				Adjusted mean changes[a]				
	Initial		Final		Mean changes		ANCOVA results		
Variable	BN ($n=39$)	Sub-BN ($n=39$)	BN ($n=34$)	Sub-BN ($n=29$)	BN	Sub-BN	MD	p	95%CI	MD
Weekly frequency										
Binges	6.90 (5.6)	1.20 (3.5)	1.10 (1.20)	2.00 (3.70)	−6.40	−0.90	−5.540	<.0005	−7.540	−3.540
Vomits	7.50 (6.9)	2.90 (6.0)	1.00 (1.70)	2.40 (4.09)	−5.90	−2.06	−3.880	.0010	−5.920	−1.850
Laxatives	6.40 (16.0)	1.40 (4.0)	2.50 (8.00)	0.48 (1.70)	−6.50	−2.32	−4.200	.0010	−6.490	−1.910
Diuretics	1.00 (2.9)	1.00 (3.4)	0.77 (2.80)	0.11 (0.58)	−0.51	−0.91	0.395	.7470	−2.120	2.920
BMI	12.90 (2.6)	21.90 (2.4)	23.20 (2.40)	22.00 (2.40)	0.04	0.14	−0.098	.5520	−0.438	0.242
EAT total	83.50 (19.9)	47.20 (24.4)	35.20 (23.30)	35.00 (25.60)	−19.8	−12.10	−7.690	.2720	−21.900	6.530
EDI-2 total	113.00 (47.2)	96.50 (40.4)	84.70 (48.80)	73.10 (40.20)	−29.4	−25.80	−3.590	.8210	−37.000	29.800
BITE										
Symptom.	24.80 (4.1)	21.30 (5.7)	20.60 (7.90)	16.30 (7.40)	−4.54	−2.80	−1.710	.5520	−7.630	4.200
Severity	15.90 (7.0)	10.80 (7.5)	9.60 (7.10)	6.00 (5.40)	−6.83	−3.20	−3.630	.1210	−8.310	1.050
SAD total	13.60 (9.4)	13.50 (7.3)	10.80 (9.70)	12.20 (8.90)	−0.48	−2.80	2.330	.3840	−3.430	8.090
SCL-90-R										
GSI	1.81 (0.8)	1.49 (0.7)	1.40 (0.90)	1.20 (0.80)	−0.28	−0.36	0.074	.7680	−0.442	0.590
PSDI	2.33 (0.6)	2.12 (0.6)	2.00 (0.66)	1.90 (0.72)	−0.23	−0.27	0.044	.8560	−0.460	0.549
PST	66.50 (18.8)	60.90 (18.7)	54.70 (25.70)	50.00 (24.80)	−7.67	−10.00	2.330	.7650	−13.700	18.400

Note. ANCOVA = analysis of covariance; BN = bulimia nervosa; MD = mean difference; CI = confidence interval; BMI = body mass index (ratio: kg/m^2); EAT = Eating Attitudes Test; EDI-II = Eating Disorders Inventory; BITE = Bulimic Investigatory Test, Edinburgh; SAD = Social Avoidance Distress Scale; SCL-90-R = Symptom Checklist-90-Revised; GSI = global severity index; PSDI = positive symptom distress index; PST = positive symptom total.

[a]Results adjusted by frequency of binge eating and purging at baseline. Change = difference between pre post values.

Secondary outcome variables: psychological, personality, comorbid psychopathology, and treatment adherence. There were no other significant differences in mean changes on other total scores in clinical, psychopathological and personality features across diagnoses. Regarding the subscales of the EDI-2 and the SCL-90-R, the only statistically significant difference was found for the EDI-2 Impulse Regulation subscale (mean reduction was 4.3 for full BN and 0.43 for sub-BN; $p = .045$). Comparisons between groups for treatment adherence showed that 19.4% (full-BN group = 13.5% and sub-BN group = 25.7%) of the patients had dropped out from treatment. Even though almost twice as many sub-BN patients dropped out from treatment compared with full-BN patients, this difference was not statistically significant (odds ratio = 0.94; $p = .960$). Because no follow-up of these patients had been conducted, reasons for dropout could not be assessed. Finally, no significant differences between the groups on number of sessions attended (adjusted mean: full BN = 5.4 vs. sub-BN = 4.6; $p = .084$) could be detected. There were no harms or adverse events associated with treatment. No patient had to be withdrawn from the psychoeducational intervention or given inpatient or medication treatment.

Discussion

The current study is a novel contribution to the literature by comparing outcome of a brief psychoeducational program on full- and sub-BN patients and addresses several fundamental issues.

The first main finding was that, although generally full BN and sub-BN are currently considered separate diagnostic categories (APA, 2000a, 2000b), with the exception of symptom severity (frequency of binge eating and vomiting) and the depression and anxiety scores, no significant differences were observed at baseline between the groups on other eating disorder symptoms or psychopathological or personality traits. This suggests that the sub-BN form of EDNOS may represent a continuum of severity rather than a discrete diagnostic entity. The fact that 69% of individuals with sub-BN had met full criteria in the past suggests the importance of considering a stage of illness classification that accounts for changes in symptom severity over time rather than necessitating a switch to a different diagnostic classification (Crow, Agras, Halmi, Mitchell, & Kraemer, 2002).

Second, in terms of therapy outcome, we observed that, after a brief psychoeducational intervention, there were significant differences in symptom change for our primary outcome variables. A significant reduction in binge eating and vomiting frequency was observed for both groups after treatment. Specifically, the full-BN patients reduced the number of weekly bingeing episodes by, on average, 6.4, whereas the sub-BN patients only achieved a mean reduction of 0.9 episodes. This reflects in part the greater initial symptomatology in full-BN patients and the fact that they had more room for improvement. Conversely, when the abstinence rates by the end of therapy were assessed for both groups, no significant differences between full- and sub-BN groups were detected either on binges (33.3% and 39.8%, respectively) or on vomiting episodes (57.3% and 62.5%, respectively). Conversely, frequency of laxative use revealed significant differences between the two groups after treatment. These results indicate that both groups profit from the same psychoeducational intervention. In relation to full BN, research has shown that psychoeducation is a useful first intervention for individuals with mild to moderate full BN, as previously reported by others (Daley & Hartman, 1999; Davis et al., 1990; Fernández-Aranda et al., 1998, 2004; Olmsted, Kaplan, Rockert, & Jacobsen, 1996). Conversely, for sub-BN, this is, to our knowledge, the first study that has tested such a psychoeducational treatment program. As noted by others (Fairburn & Harrison, 2003; Grilo et al., 2003), our findings argue that the clinical management of sub-BN need not differ from that of full BN.

In relation to our secondary therapy outcome variables, no significant differences in symptom change were found for most of the psychopathological and personality features. The only exception was found on the Impulse Regulation subscale of the EDI-2, in which a significant reduction for both groups was observed after treatment. The full-BN group exhibited more change for these variables than the sub-BN group. The brief psychoeducational group therapy we applied in our study yielded a dropout rate of 19.4% (full-BN group = 13.5%, sub-BN group = 25.7%). These results are somewhat lower than those reported in other studies (17.2–27.3%; McKisack & Waller, 1997). As we have indicated in previous work (Fernández-Aranda et al., 1998), two factors account for this discrepancy. First, the psychoeducational intervention is brief and perhaps less prone to dropout. Second, we provide motivational work with our patients before initiating therapy, which could improve adherence. Despite the absence of statistical significance, it should be acknowledged that almost twice as many patients from the sub-BN group (13.5% vs. 25.7%) dropped out. Research has shown that adherence to treatment is related to motivation to change in eating disorders (Ametller, Castro, Serrano, Martinez, &

Toro, 2005). Accordingly, previous studies have indicated a lower motivation to change in EDNOS patients compared with BN and AN individuals (Casasnovas et al., 2007). This differential resistance to treatment observed between eating disorder subtypes may be related to low self-efficacy and passive attitude to their own capacity to change (Blake, Turnbull, & Treasure, 1997) and differences in decisional balances (pro–cons) vis-à-vis their current situation (Cockell, Geller, & Linden, 2002).

The results of the present study have various clinical implications. First, brief psychoeducational interventions appear to confer benefit for both individuals with full BN as well as sub-BN. Second, with the exception of severity of eating disorder symptoms, few differences emerged between those with full BN or sub-BN on clinical, personality, or outcome variables.

This study does have some limitations. First, the sample size was relatively small. Although few significant differences were observed between the two groups, this does not mean that differences would not emerge with large samples or with different definitions of sub-BN. Second, we reported a 2-week abstinence period rather than a 4- or 8-week period because of the brief nature of the intervention: A longer period of abstinence is needed to ensure stability of change. Third, although the literature has shown little effect of no treatment in BN (Fernández-Aranda et al., 1998), in sub-BN data are lacking as to the impact of a no-treatment or placebo control. Fourth, we report no medium- to long-term follow-up data. Because we only assessed the participants at the termination of the short intervention, there is no way of knowing whether these effects persist over time.

Future studies should aim to overcome these limitations and should also include follow-up durations of at least 6 months to 1 year. Finally, replicating the present study in a group therapy of longer duration could clarify predictors of various forms of treatment within the EDNOS category.

To summarize, this study has shown that, first, full-BN and sub-BN share common psychopathological symptoms and personality traits. Second, no differences in therapy outcome, after a brief group approach, were observed for the two groups in terms of general eating disorder symptomatology and psychopathology. On the basis of results from the present study, it can be concluded that both individuals with threshold and sub-BN profit from brief psychoeducational interventions.

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8.9. Study 9

Blindness and Bulimia Nervosa: A Description of a Case Report and its Treatment

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INTRODUCTION

Over the last few decades, many authors have postulated the essential role of body image in the etiology of eating disorders (ED). However, other authors have questioned the etiopathologic value of this concept (1) because they believe that other triggering factors are involved in the development of ED, in particular in Bulimia Nervosa (BN) (2-3). Blindness has rarely been described in the ED literature. In case reports in which this condition has been reported before an ED, it was concluded that visual body image was not essential for the development of the ED. This is the first report in which bulimia nervosa (BN) and its treatment in a blind woman were described.

OBJECTIVES

To report the first reported case of BN and its treatment (cognitive-behavioral oriented) in a blind participant.

CASE RESPORT

- A blind, 47-year-old woman developed the complete clinical picture of BN (purging subtype). Since the age of 43 years (onset of the ED), the patient described the presence of two to four weekly binging and vomiting episodes, which were frequently triggered by psychosocial stressors.
- From a behavioral point of view, the patient presented with low self-esteem and deficits in social and problem-solving skills, which were the result of the interpersonal conflicts she had with her family, especially with her children.
- These variables appear to have contributed to the patient's vulnerability to escape (after a negative reinforcing scheme) from problems by means of binging and vomiting, which are considered to be inappropriate coping strategies.

PHYSICAL EXAMINATION

- The patient became blind during her infancy due to a congenital illness of unknown etiology (possibly infectious).
- The physical exploration and the anamnesis with specific devices did not show any relevant findings.

PERSONAL ANTECEDENTS

- The patient was the younger of two children (both girls).
- No parental mental disorders were detected.
- She had been married for 9 years to her husband and had 2 children (a woman of 25 years and a man of 18 years) from a previous marriage.

TREATMENT

- Twenty-one weekly outpatient cognitive-behavioral sessions plus 4 follow-up sessions (at 1, 3, 6, and 12 months) were conducted.
- The main goals of the therapy were to increase her motivation, complete a behavioral analysis, and teach behavioral techniques such as coping with stress and solving problems (in spite of escaping from them by binging).
- Due to the patient's symptoms, we decided to conduct non–symptom-oriented cognitive-behavioral therapy (CBT). More than paying attention to the eating symptoms, the therapy was basically centered in the behavioral and emotional background deficits of the patient.

  Therefore, the following techniques were used:
  - motivational interviewing,
  - awareness of the "binging-escaping from problems" vicious circle,
  - coping with negative emotions,
  - social and problem-solving skills,
  - and couple or family counseling.

RESULTS

- A dramatic reduction in eating symptoms was observed after the maintaining or triggering factors (individual deficits and interpersonal reactions of the family members) had been reduced.
- During treatment, the rate of binge eating and the consequent vomit episodes started to decline after the 4th session, whereas abstinence of binging and vomiting occurred after the 11th session. At 6 and 12 months of follow-up, the patient was still abstinent from ED symptoms.

CONCLUSIONS

In the current case, the onset of the patient's ED was not associated with her body shape dissatisfaction, but with her inadequate coping skills. The therapy employed (non–symptom-oriented CBT) demonstrated that flexible ED treatment programs, which try to adapt to the different facets of the patient's ED symptoms, are able to yield favorable results.

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CASE REPORT

Blindness and Bulimia Nervosa: A Description of a Case Report and its Treatment

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ABSTRACT

Objective: Blindness has rarely been described in the eating disorder (ED) literature. In case reports in which this condition has been reported before an ED, it was concluded that visual body image was not essential for the development of the ED. This is the first report in which bulimia nervosa (BN) and its treatment in a blind woman were described.

Method: We report a single diagnosed and treated case of BN in a blind, 47-year-old Spanish woman. This case presented as its main characteristics the late onset of the ED, restrictive dieting, binging, and consequent purging behavior characterized by vomiting and great difficulties of coping with stress. From the beginning, the woman's body image was not essential. The treatment consisted of 21 individual outpatient sessions, which followed a non–symptom-oriented cognitive-behavioral approach, in which problem solving and stress management strategies were employed.

Results: Before, after the treatment, and at the 6-month and 1-year follow-up, the clinical evolution of the patient was assessed.

Conclusion: Although a few descriptions of single case reports on blindness in individuals with anorexia nervosa (AN) have already been reported in the literature, to the authors' knowledge, this is the first reported case in which this condition and its treatment have specifically been reported in an individual with BN.

Keywords: bulimia nervosa; blindness; eating disorder; body image; case report

(Int J Eat Disord 2006; 39:263–265)

Introduction

Over the last few decades, many authors have postulated the essential role of body image in the etiology of eating disorders (ED). However, other authors have questioned the etiopathologic value of this concept[1] because they believe that other triggering factors are involved in the development of ED, in particular in bulimia ervosa (BN).[2–4]

In blind individuals, specific problems and disorders, such as behavioral and emotional problems,[5,6] sleep-wake disorders,[7] suicide, and depression,[8,9] have frequently been described. Most of these reports have focused on children and adolescent populations. The few studies that assessed the mental status of blind adult participants described patients as being characterized by low self-esteem, symptoms of depression, and poor strategies of coping with stress.[10] When congenitally blind women were compared with women blinded later in life, the former showed less body dissatisfaction,[11] which indicates that the ability to visualize oneself and others is integrally linked to a person's body dissatisfaction and, consequently, may promote disordered eating attitudes.

In the literature, several cases of blindness have already been reported before the onset of anorexia nervosa (AN).[12–15] The main hypothesis of these case reports was that body image preoccupations were not essential for the development of AN. To the authors' knowledge, this is the first reported case of BN and its treatment (cognitive-behavioral oriented) in a blind participant.

Case Report

The Ethics Committee of the University Hospital of Bellvitge (Barcelona, Spain) approved this study and informed consent was obtained from the patient. According to criteria in the 4th ed. of the Diagnostic and Statistical Manual of Mental Disor-

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ders (DSM-IV; Washington, DC: American Psychiatric Association; 1994), a blind, 47-year-old woman developed the complete clinical picture of BN (purging subtype). Since the age of 43 years (onset of the ED), the patient described the presence of two to four weekly binging and vomiting episodes, which were frequently triggered by psychosocial stressors. The patient did not show any impulsive behavior, alcohol use, or drug abuse. She was overweight (90 kg, 1.57 m, body mass index [BMI] = 36.6) and wished to be thinner (ideal BMI = 28.4), not because of shape concerns, but because of physical reasons. In addition, due to psychosocial stressors, anxious and depressive symptoms were constantly present. During the last 4 years, the patient had gained >30 kg. Before this weight gain, the patient had exhibited a lower weight (BMI = 25.6) and revealed that during the time when she was thinner, she neither exhibited any body image concerns nor wanted to lose weight.

From a behavioral point of view, the patient presented with low self-esteem and deficits in social and problem-solving skills, which were the result of the interpersonal conflicts she had with her family, especially with her children. These variables appear to have contributed to the patient's vulnerability to escape (after a negative reinforcing scheme) from problems by means of binging and vomiting, which are considered to be inappropriate coping strategies. According to the DSM-IV criteria, the patient presented the following Axis I diagnoses: BN and dysthymia.

Physical Examination

The patient became blind during her infancy due to a congenital illness of unknown etiology (possibly infectious). She did not present other medical antecedents of interest except allergic asthma to treatment with bronchodilatators. Furthermore, the patient exhibited 2–3 daily semiliquid excretions for >3 years, which changed according to emotional factors. The physical exploration and the anamnesis with specific devices did not show any relevant findings. The biochemical profile, including hepatic function, renal function, and the concentration of ions, ferritin, iron, and vitamin B 12, proved to be within normal parameters of functioning. There were no alterations in the blood cell count, level of thyroid hormones, examinations of coagulation, gastrointestinal transit, endoscopy, and abdominal ultrasound scan. The lactose test result was negative. By means of coprocultive methods, no pathogenic agents, which could have explained the symptoms, could be detected. Celiac illness was excluded by means of the determination of Ac Ig Antiendomisio (IFI technique with monkey esophagus), Ac Ig A antigliadin (enzyme-linked immunosorbent assay [ELISA] technique), Ac Ig A antitransglutaminasa (ELISA technique), and normal values in the serum levels of IgA. The medical diagnostic orientation was an irritable colon, and other possible gastrointestinal pathologies such as the malabsortion syndrome, which could have explained the symptoms.

Personal Antecedents

The patient was the younger of two children (both girls). No parental mental disorders were detected. She had been married for 9 years to her husband and had 2 children (a woman of 25 years and a man of 18 years) from a previous marriage.

Treatment

Twenty-one weekly outpatient cognitive-behavioral sessions plus 4 follow-up sessions (at 1, 3, 6, and 12 months) were conducted. The main goals of the therapy were to increase her motivation, complete a behavioral analysis, and teach behavioral techniques such as coping with stress and solving problems (in spite of escaping from them by binging). Due to the patient's symptoms, we decided to conduct non–symptom-oriented cognitive-behavioral therapy (CBT). More than paying attention to the eating symptoms, the therapy was basically centered in the behavioral and emotional background deficits of the patient. Therefore, the following techniques were used: motivational interviewing, awareness of the "binging-escaping from problems" vicious circle, coping with negative emotions, social and problem-solving skills, and couple or family counselling. A dramatic reduction in eating symptoms was observed after the maintaining or triggering factors (individual deficits and interpersonal reactions of the family members) had been reduced. During treatment, the rate of binge eating and the consequent vomit episodes started to decline after the 4th session, whereas abstinence of binging and vomiting occurred after the 11th session. At 6 and 12 months of follow-up, the patient was still abstinent from ED symptoms.

Conclusion

In the current case, the ED seems to be a consequence of inappropriate coping skills with stress. Indeed, patients who present some behavioral handicaps or deficits are more vulnerable to the development of an ED.[5,9] As reported in the literature, in many of those cases, the ED is not due to

an overemphasis on physical attractiveness, but to a personal difficulty to cope with stress.[16] In the current case, the onset of the patient's ED was not associated with her body shape dissatisfaction, but with her inadequate coping skills.[2] The therapy we employed (non–symptom-oriented CBT) demonstrated that flexible ED treatment programs, which try to adapt to the different facets of the patient's ED symptoms, are able to yield favorable results.

This is the first report to describe the clinical picture and therapy of a blind woman with BN.

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9. DISCUSSION

The overall objective of the present thesis was to improve the health of women with EDs by using multifaceted translational research. In order to achieve this we assessed three areas of ED research. The first line of investigation assessed the comorbidity of substance use in EDs **(Studies 1 to 3)**. The second area examined psychological, behavioural and environmental correlates of EDs **(Studies 4 to 7)**. Finally the third line of research assessed the effectiveness of different therapeutical interventions in EDs **(Studies 8 to 9)**. We will try to discuss each of the main findings in more detail and put them into a new theoretical framework. The results of the present thesis will hopefully help guide the direction of research in the field of risk factors of EDs and contribute to the prevention and treatment of EDs.

9.1. Comorbidity of substance use in eating disorders

The first three studies **(Studies 1 to 3)** evaluated the comorbidity of substance use in EDs. The aim of our first study, a meta-analysis **(Study 1),** was to systematically estimate the direction and the strength of the association between EDs and drug use (DU) across sixteen published studies. The meta-analysis was carried out initially clustering all types of EDs together, with a global measure of DU followed by an analysis of specific drug and ED subtypes. The purpose of our second study **(Study 2)** was to assess lifetime substance abuse, family history of alcohol abuse/dependence and novelty seeking in three different ED groups [(AN-R; AN-BP and AN who cross over to BN (AN-Cross)]. Finally, the goal of our third study **(Study 3)** was to compare differences in lifetime and current tobacco, alcohol and DU of a wide range of drug classes and ED diagnoses across five different European countries. The results of these studies suggest that a.) substance use is higher in individuals with EDs than healthy controls **(Studies 1 and 3)**, b.) that the presence of a lifetime history of substance use may be particularly prevalent in patients with bulimic characteristics **(Studies 1 to 3)** and c.) that EDs and substance abuse may represent expressions of a fundamental predisposition to addictive behaviour possibly related to the genetically influenced trait of novelty seeking **(Study 2)**.

Finally, our third study **(Study 3)** also revealed some cross cultural differences on this topic.

9.1.1. Substance use in eating disorders and healthy controls

In two of our comorbidity studies **(Studies 1 and 3)** we observed that EDs exhibited higher rates of general substance use than healthy controls. This finding is in agreement with previous reviews on substance use in EDs (Holderness et al., 1994; Pirim & Ikiz, 2004; Wolfe & Maisto, 2000). The nature of this comorbidity remains however unknown (Krahn & Gosnell, 1991; Wiederman & Pryor, 1996). Overlaps between the pathways in the brain for food intake and drug addictions suggest that an imbalance in the chemical transmitters of the reward pathways may be responsible for this co-occurrence (Colantuoni, Rada, McCarthy, Patten, Avena,& Chadeayne et al., 2002; Dimitriou, Rice, & Corwin, 2000).

9.1.2. Substance use in specific subgroups of eating disorders

All our substance use studies **(Studies 1 to 3)** indicated that substance use was highest in individuals suffering from bulimic behaviours - a result that mirrors a trend of greater substance use among patients with binge-purging symptomatology, which has also frequently been observed in earlier investigations (Blinder et al., 2006; Bulik, Klump, Thornton, Kaplan, Devlin, Fichter et al., 2004; Gadalla & Piran, 2007; Peñas-Lledó, Sancho & Waller, 2002a).The development of animal models has helped understand the overlap between these behaviours. Animals “binge eat” if they are exposed to some of the environmental factors considered to be important to human EDs (e.g., food restriction, alternating exposure to palatable food etc.) (Avena, Long, & Hoebel, 2005; Corwin, 2006; Lewis, Rada, Johnson, Avena, Leibowitz, & Hoebel, 2005; Treasure, in press). These “binge priming” conditions affect the hedonic characteristics of appetite regulation and hence lead to an over sensitized reward arrangement which may than progress into difficulties with addictive behaviours (Avena & Hoebel, 2003; Koob & Le Moal, 2005; Robinson & Berridge, 2003; Thiele et al., 2004; Treasure, in press).

9.1.3. Personality traits in eating disorder individuals with substance use

The increased risk of substance abuse in people with bulimic symptomatology might also be related to differences in temperament such as an increased novelty seeking. Correspondingly, in our second study **(Study 2)** we revealed that novelty seeking (a reward related construct) was significantly associated with substance use in the AN-BP and AN-Cross groups but not the AN-R group, which is in line with other studies (Fernandez-Aranda et al., 2006; 2008). Novelty Seeking has been linked to particular neurochemical correlates, i.e., norepinephrine deregulation (Cloninger, 1987; Ham, Choi, Lee, Kang, & Lee, 2005) and dopaminergic disturbances (Cloninger, 1987; Keltikangas-Jarvinen, Puttonen, Kivimaki, Rontu, & Lehtimaki, 2006). Even though specificity of the correlates is uncertain, our results propose new ways to examine the relationship between certain personality traits and biological performance.

Impulsivity could be another candidate feature to help explain the comorbidity of EDs and substance use (Fernandez-Aranda et al., 2008; Peñas-Lledó, Vaz, Ramos, & Waller (2002b). Accordingly, in the literature the concept of "multi-impulsive" BN is widely used to depict those individuals with elevated impulsiveness and higher comorbidity with various substances as well as other impulsive behaviors such as self-harming behaviours, suicide, compulsive buying etc. (Lacey, 1993; Matsunaga, Kirriike, Iwasaki, Miyata, Matsui, & Nagata et al., 2000; Nagata, Kawarada, Kiriike, & Iketani, 2000).

9.1.4. Comorbidity of various substances and eating disorders

In agreement with the current literature (Baker & Kendler, 2007; Baker, Piper, McCarthy, Majeskie, & Fiore, 2004), in our third study **(Study 3),** we revealed that individuals who have an ED and utilize psychoactive substances are at a significantly higher risk than the general population to develop (or to have developed) psychological and behavioural patterns that leave them vulnerable for displaying other addictive disorders (e.g. utilizing various substances

simultaneously as it was the case in **Study 3**). Consequently, many researchers have proposed that an addictive personality is an underlying trait that predisposes individuals to both EDs and substance use (Holderness et al., 1994). However, empirical evidence about the existence of such an "addictive personality" is as yet inconclusive (Holderness et al., 1994).

9.1.5. Family history of substance use in eating disorders

The comorbidity of substance use in ED patients raises important concerns as to how these disorders are transmitted. The results from our second study **(Study 2)** showed that a family history of alcohol abuse/dependence was significantly higher in the AN-BP and AN-Cross groups than in the AN-R individuals. The fact that genetic factors appear to play a role in the development of both EDs and substance use, therefore leads us to consider that a genetic contribution to the comorbidity of both disorders exists. Previous studies have already shown that a predisposition to alcoholism seems to be genetically transmitted (Bushnell, Wells, & Oakley-Browne, 1996; Goldbloom, Naranjo, Bremner, & Hicks, 1992; Kaye & Wisniewski, 1996). However, the possibility of a genetic predisposition to other types of substances has only recently begun to receive attention (Redgrave, Coughlin, Heinberg, & Guarda, 2007).

9.1.6. Specific forms of substance use in people with eating disorders

When specific types of substances were assessed individually we documented raised levels of opiates-cannabis and general illicit drugs in our meta-analysis (**Study 1)** and the employment of legal and illegal drugs to influence weight and appetite in our third study **(Study 3)**. These results are in accordance with some former studies (Herzog, Franko, Dorer, Keel, Jackson, & Manzo 2006; Nappo, Tabach, Noto, Galduroz, & Carlini, 2002) and suggest that ED patients utilize various types of substances and not just only appetite suppressant drugs as previously anticipated. Central nervous system stimulants, such as amphetamines or cocaine, might be employed to suppress appetite. However, since these drugs generally extend habitual phases of restlessness, users might also turn to opiates, sleeping pills, or tranquilizers, to cancel out these undesired

side effects (Nappo et al., 2002). Our results therefore indicate that it is imperative to differentiate between distinct classes of substances when assessing comorbidity of substance use in EDs.

9.1.7. Cross-cultural comparison on substance use in eating disorders

In our third study **(Study 3)** some differences across countries in the comorbidity of EDs and substance use emerged, with the UK and Spain generally revealing the highest prevalence rates of tobacco and general DU, which parallels the findings from a current report on drug consumption in European populations (EMCDDA, 2007). This cross-cultural variation might be attributable to macro-level factors such as the socio-cultural context, the existing legislation of drugs, the accessibility of drugs, opinion and attitudes towards drugs and the socioeconomic situation of the country (Wittchen & Jacobi, 2005).

9.2. Psychological, behavioural and environmental correlates of eating disorders

9.2.1. An animal model of binge eating behaviour

In our fourth study **(Study 4)** we tested whether a specific context could elicit eating in rats as a result of classical conditioning and whether this effect depended on the caloric density of food. The main result of this research was that context-potentiating of eating was found in the high-density (HD) groups, but not in the low-density (LD) groups. The present finding is important in replicating an effect-context-potentiated eating- that has been little investigated and yet- as argued in our paper- may be extremely important for understanding binge eating behaviour in ED patients. The failure to detect the effect in the LD groups may have been because of sensory differences between the two foods, including one being a solid food and the other a liquid, rather than caloric density. Alternatively, it could be possible that the non-conditioned context had become an inhibitory cue for eating since food had never been available in this context.

9.2.1.1. Energy density of food

The HD groups in our study received HD food during conditioning sessions and LD food during maintenance sessions. This pattern of eating has similarities with that observed in individuals with binge eating behaviour. Individuals with EDs tend to eat HD food during their binges, whereas during non-binge meals they generally consume fewer calories than healthy controls (Alpers & Tuschen-Caffier, 2004; Stein, Kenardy, Wiseman, Dounchis, Arnow & Wilfley, 2007). It is possible that such self-dieting can lead to energy deprivation in these people. Then, HD food could signal a regain of such energy loss and therefore its cues could become more easily associated with a specific context, which in turn could lead to overeating (Jansen, 1998; Overduin, Jansen, & Eilkes, 1997).

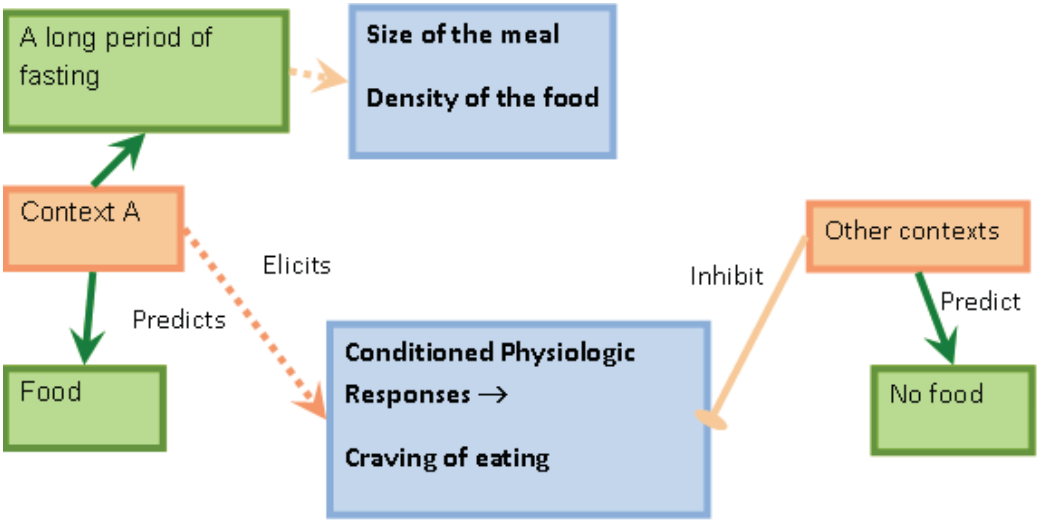
9.2.1.2. Time elapse

The bigger consumption in the conditioned context observed in the present study could also be attributed to the anticipation of a long elapse of time until the next meal. In the present experiment rats received food every 23 hours during the first 5 conditioning days and every 9 and 15 hours during the last 5 days. It is therefore possible that contextual cues anticipated a long inter-meal period in the present experiment and that this in turn could have been responsible for the ingestion of the large amount of food which was observed in the animals when tested in the conditioned context. This is in accordance with previous studies conducted with rats (White, Mok, Thibault, & Booth, 2001) and humans (Birch, McPhee, Sullivan, & Johnson, 1989). Therefore, if binges generally occur in the same context (place, time of day, thoughts, etc.), these cues could be associated not only with physiological conditioned responses but also with the anticipation of a long elapse of time until the next meal (e.g. from dinner time to the next lunch time).

9.2.1.3. An extended model of learning for binge eating

The present findings also provide support for the classical conditioning model proposed by Jansen (1998). However, our results suggest that the cue reactivity theory could incorporate two more factors to account for bingeing behaviour, which are: a) that other contexts could be associated with the absence of food and then inhibit the physiological responses and the craving for eating and b.) that the conditioned context could anticipate a long fasting period that produces overeating. This extended model of learning for binge eating is represented in *figure 12.*

Figure 12: *An extended model of learning for binge eating*



9.2.2. Individual and family eating patterns during childhood

Studies 5 and 6 assessed the association between early individual and family eating patterns and the development of a later ED. In addition **Study 6** examined whether these patterns differed across various European countries. In our fifth study **(Study 5)** all the items from the "Early Eating Environmental Subscale" of the Cross Cultural (Environmental) Questionnaire (CCQ) were employed. Our

findings indicated that eating excessive sweets and snacks and consuming food specially prepared for the respondent were positively related to a subsequent ED while consuming regularly breakfast was negatively associated with an ED. In **Study 6** we decided to provide an empirical reduction of this scale by employing a CatPCA. Analyses indicated that the new adjusted domains with the strongest positive associations with EDs in the total sample were: "food used as individualization" and "control and rules about food". On the other hand we revealed that healthy eating was negatively related to a subsequent ED. Only some difference across ED subtypes were obtained in both studies. Finally, in **Study 6** only a few cross-cultural differences were uncovered.

9.2.2.1. Eating excessive sweets and snacks

In **Study 5** we found that eating excessive sweets and snacks was related to a subsequent ED. Our results support previous studies which have shown that recent changes in eating habits have led to a decline in traditional meal eating and an increase in snacking, with multiple eating episodes spread throughout the wole day (Bellisle, McDevitt, & Prentice, 1997).

9.2.2.2 Food used as individualization-food especially prepared for the respondent

Furthermore, the results from **Study 5** indicated that food especially prepared for the patient was related to the development of a subsequent ED. Similarly in **Study 6** this item, which was summarized in the domain "food used as individualization", was also associated with a later ED. The need for individualized foods within the family (e.g. father, siblings and own patients) might be related to the increased risk of EDs within the family by decreasing social bonding. Separation-individuation is a core issue for many individuals with EDs, especially in older adolescents. Accordingly studies have shown that compared to younger adolescents, older youngsters reported less frequent family meals, fewer rules at mealtimes, and a greater difficulty in scheduling family meals (Neumark-Sztainer, Story, Hannan, Perry, & Irving, 2002). Hence these findings indicate that it is essential to take the patient´s age as well as his/her

actual stage in the family lifecycle (e.g., the "leaving home "phase) into consideration when assessing eating patterns.

9.2.2.3. Control and rules about food

"Control and rules "about food increased the probability of presenting a later ED in **Study 6**. Correspondingly, previous studies have indicated that parents play an active role in their children´s emerging dietary restraint by controlling provision and restriction of specific foods (Birch & Fisher, 1998; Brown & Ogden, 2004; Edmunds & Hill, 1999; Fisher & Birch, 1999a., 1999b; Ogden, Reynolds, & Smith, 2006). In addition, there is some evidence that parents with EDs may restrict certain types of food from their children, which has been attributed to the parents' concerns about body size being projected onto their child (Edmunds & Hill, 1999; Faith, Berkowitz, Stallings, Kerns, Storey & Stunkard, 2006; Faith & Kerns, 2005; Russell, Treasure, & Eisler, 1998).

9.2.2.4. Healthy eating - consuming breakfast

In **Study 5** consuming regularly breakfast was negatively linked to the development of an ED. This item was comprised in the category of "healthy eating" in our sixth study **(Study 6)** and accordingly also diminished the probability of developing a later ED. In line with our results preceding studies have also shown that children and adolescents who reported more regular and structured family meals [(including eating breakfast (Evers, Taylor, Manske, & Midgett, 2001; Lattimore & Halford, 2003)], an encouraging environment at family meals and a high priority for family meals (Franko, Striegel-Moore, Thompson, Affenito, Schreiber, & Daniels et al., 2008; Fulkerson, Story, Mellin, Leffert, Neumark-Sztainer, & French, 2006; Neumark-Sztainer, French, Hannan, Story, & Fulkerson, 2005: Sjoberg, Hallberg, Hoglund, & Hulthen, 2003) were less likely to present disturbed eating behaviours (Genders, Treasure, Fernandez-Aranda, & Tchanturia, 2008) and were more probable to have a positive psychosocial development (Neumark-Sztainer et al., 2000; Neumark-Sztainer, Wall, Story, & Fulkerson, 2004).

9.2.2.5. Differences across eating disorder subtypes in early eating behaviour

Only a few significant differences across ED subdiagnoses emerged in both studies **(Studies 5 and 6)**. In **Study 5** we found that having grandparents living at home, having food specially prepared for the respondent and eating a lot of snacks increased the chances of developing AN. Conversely, having food specially prepared for the respondent and eating a large amount of snacks, along with the father placing greater amount of value on food and healthy eating, increased the likelihood of displaying BN. In accordance with previous studies, these findings highlight the importance of the wider family, not just the mother, in the development of EDs (e.g. Botta & Dumlao, 2002). The fact that the respondents in this study reported requiring food specially prepared for them in childhood implies that they may already have had feeding difficulties as a child (Genders, Treasure, Fernandez-Aranda, & Tchanturia, 2008).

9.2.2.6. Cross-cultural comparisons in early eating behaviour

The results from **Study 6** indicate that only a few consistent differences across countries emerged, which might be due to the fact that even though there appear to be "traditional cultures of eating habits" across EU countries, globally there seem to be modern ones, such as "fast food restaurants" which have started to enter our everyday life (Dowler, 2001; Irala-Estevez, Groth, Johansson, Oltersdorf, Prattala, & Martinez-Gonzalez, 2000).

9.2.3. Anger expression in eating disorders

Study 7 aimed to compare anger expressions in people with EDs and non-eating disordered controls. Furthermore, this study also aimed to explore the relation between ED symptoms, comorbid psychopathology, personality traits and impulsive behaviours. Results indicated that women with EDs obtained significantly higher mean scores than the controls on all State Trait Anger Inventory-2 (STAXI-2) subscales except for the Anger Control scale. When various purging methods were assessed independently, the frequency of laxative

use was associated with anger suppression. Eating disordered symptoms and specific personality traits were positively related to different anger expressions. Finally patients with higher scores on anger suppression were more likely to report self-harming behaviours.

9.2.3.1. Anger in eating disordered individuals and healthy controls

In accordance with previous studies we revealed that ED patients reported higher anger levels than controls (Fassino et al., 2001; Fava, Rappe, West, & Herzog, 1995; Thompson, Wonderlich, Crosby, & Mitchell, 1999). This might suggest that ED patients may have inadequate anger expression and skill deficits in dealing with anger and frustration. Furthermore we revealed that ED patients with abnormal anger expression seem to present higher ED severity and more general psychopathology which is also in accordance with previous studies (Fava et al., 1995; Fernandez-Aranda et al., 2006; 2008).

The extent to which this inadequate anger expression is associated with the development and maintenance of abnormal eating patterns remains however unclear. Anger and aggression are multifaceted phenomena that are intensely influenced by environmental and developmental factors. Hyposerotonergic functioning and noradrenergic dysregulation, have been assumed to be the biological substrate for anger (Rosenbaum, Fava, Pava, McCarthy, Steingrard, & Bouffides,1993; Truglia et al., 2006) and have often been observed in ED patients (Heufelder, Warnhoff, & Pirke, 1985; Jimerson, Lesem, Hegg, & Brewerton, 1990; Kaye & Weltzin, 1991). As regards to the environmental contributing factors, studies have implicated that victims of violent behaviour during childhood commonly suffer from inadequate anger manifestations and EDs in adulthood (e.g. van der Kolk & Fisler, 1994).

9.2.3.2. Anger and purging behaviour in eating disorders

In line with previous studies we found that laxative use was related to anger in general (Tozzi, Thornton, Mitchell, Fichter, Klump, & Lilenfeld et al., 2006)

and to anger suppression in particular (Truglia et al., 2006; Waller, Babbs, Milligan, Meyer, Ohanian & Leung, 2003). Different purging methods may therefore be related to different facets of anger as suggested by previous studies (Reba, Thornton, Tozzi, Klump, Brandt, & Crawford et al., 2006; Vaz, Peñas, Ramos, Lopez-Ibor & Guisado, 2001). It can therefore be hypothesized that bulimic behaviours serve different emotional functions with a particular contrast between the facets of anger that are influenced by "fast-acting" behaviours (e.g. bingeing, vomiting, exercise) and those that are influenced by "slow-acting" behaviours (e.g. laxative abuse).

9.2.3.3. Anger and personality in eating disorders

Finally in relation to personality, various significant relationships were found between the general Anger Expression Index and some personality traits, namely harm avoidance and reward dependence. This contradicts previous studies which have shown no relationship between personality, disordered eating and different ways of managing aggressive feelings in ED individuals (Fassino et al., 2001). As expected, harm avoidance, commonly found in individuals with EDs (Fassino, Abbate-Daga, Amianto, Facchini, & Rovera, 2003a), was positively related to Trait Anger-Angry Reaction and Anger Expression-IN (anger supression). Contrastingly, reward dependence was found to be negatively related to Trait Anger-Angry reaction and Anger Expression-In. This seems logical as individuals who rely on others for approval and reward are unlikely to view outwardly directed anger to be in service of those interpersonal goals.

9.2.3.4. Anger and impulsive behaviours in eating disorders

Finally we revealed that patients who felt an intense urge to express anger also displayed a variety of impulsive self-harming behaviours. In agreement with our findings numerous studies (Favaro & Santonastaso, 1998, 1999, 2000; Fernandez-Aranda et al., 2008; Peñas-Lledó, Fernández, & Waller, 2004; Truglia et al., 2006) have observed impulse control deficits, including anger, in women with EDs and have therefore suggested that these behaviours operate as

a coping strategy for the self-regulation of negative emotions, hyperarousal and/or dissociative conditions.

9.3. Treatment effectiveness in eating disorders

The aim of our last two studies **(Studies 8 and 9)** was to assess the effectiveness of two different treatment modalities for BN and EDNOS. **Study 8** compared individuals with BN and sub-threshold BN (EDNOS) on symptoms and personality features, and examined the efficacy of a brief psychoeducational intervention for these diagnostic groups. Results indicated few differences between patients with full-syndrome versus sub-threshold BN, and a similar response to treatment. Conversely, in **Study 9** we employed a non-symptom focused treatment program to treat a blind woman with BN, whose ED symptoms were caused by interpersonal difficulties with her family. After the patient was able to deal with these stressors more effectively an automatic improvement in the ED symptomatology was observed. Both studies therefore indicate that different treatment modalities are useful for reducing ED symptomatology and associated conditions.

9.3.1. Treatment effectiveness of full (threshold) vs. sub-threshold Bulimia Nervosa

9.3.1.1. Differences in baseline characteristics

The first main finding of **Study 8** was that, although generally full BN and sub-BN are currently considered separate diagnostic categories (APA, 2000), no significant differences were observed at baseline between the two groups in terms of clinical and personality features (Fairburn & Bohn, 2005; Fairburn, Cooper, Bohn, O'Conner, Doll & Palmer, 2007b; Ricca, Mannucci, Mezzani, Di Bernardo, Zucchi, & Paionni et al., 2001). The current findings are of interest in view of the uncertainties that exist regarding the appropriate diagnostic boundary for BN (i.e., whether the diagnostic concept is too narrow as it stands) and the relative surfeit of EDNOS cases. The results of our study imply that the sub-BN form of EDNOS may stand for a continuum of gravity (rather than a

separate diagnostic entity), which may vary from mild but enduring dieting, through subthreshold conditions of vague clinical importance, to threshold cases of EDs.

The fact that most of the individuals with sub-BN met full criteria in the past provides further evidence for such a continuum and that cross-diagnostic temporal movement is common among people with EDs (Fairburn & Harrison, 2003; Milos et al., 2005). Surprisingly, the significance of this migration of patients across ED diagnoses has received surprisingly little attention in the literature (Beumont, Russell, & Touyz, 1993; Eddy et al., 2008b; Fairburn & Bohn, 2005; Tozzi, Thornton, Klump, Fichter, Halmi, & Kaplan et al., 2005). However, with this overlap and fluidity between diagnostic categories in mind, researchers have recently begun to study more broadly defined phenotypes including subthreshold cases and to focus on attitudinal and behavioural traits rather than full syndromes (Pinhero, Bulik, Sullivan & Machado, 2008).

9.3.1.2. Therapy outcome of a brief psychoeducational intervention

The brief psychoeducational intervention employed in **Study 8** appeared to have confered benefit for both individuals with full BN as well as sub-BN. In relation to full BN, research has shown that psychoeducation is a useful first intervention for individuals with mild to moderate full BN (Daley & Hartman, 1999; Davis, Olmsted, & Rockert, 1990; Fernandez-Aranda, Bel, Jimenez-Murcia, Vinuales, Turon & Vallejo, 1998; Fernandez-Aranda et al., 1998a; Olmsted et al., 1991). Conversely, for sub-BN, this is, to our knowledge, the first study that has tested such kind of treatment program. Our findings therefore argue that the clinical management of sub-BN need not differ from that of full BN, which is also in line with previous studies (Fairburn & Harrison, 2003; Grilo, Sanislow, Shea, Skodol, Stout, & Pagano, et al., 2003). However, only by further clarifying clinical syndromes within the current EDNOS category and investigating the optimal approach to treat these conditions will we be able to determine how best to treat the majority of treatment-seeking individuals.

9.3.2. Blindness and Bulimia Nervosa - A case report

In our last but not least study **(Study 9)** we employed a non-symptom-oriented cognitive-behavioural therapy (CBT) in a congenital blind woman, whose ED symptoms were not due to an overemphasize on physical attractiveness, but to a personal difficulty to cope with stress. Hence, the therapy focused on the emotional background deficiencies related to these stressors by comprising the following therapeutically techniques: motivational interviewing, awareness of the "bingeing-escaping from problems" vicious circle, coping with negative emotions, social and problem-solving skills, and couple/family counselling. Results indicated that after the maintaining or triggering factors (individual deficits and interpersonal difficulties with the family members) had been reduced, a dramatic reduction in the ED symptomatology was also obtained. These findings therefore indicate that treatment should always be tailored to the patient´s characteristics and personal needs.

9.4. An etiopathological model of eating disorders

To date, a number of more or less integrated models of ED risk factors have been put forward (e.g., Davis, 1997; Fairburn & Harrison, 2003; Garner & Garfinkel, 1980; Williamson, Netemeyer, Jackman, Anderson, Funsch, & Rabalais 1995; Stice, 2001), the majority of which share the idea that EDs are not caused by a single factor but are "multi-determined". Using some concepts of previously described nomenclatures of EDs (e.g. Garner & Garfinkel, 1980) we tried to develop a "new" model, which would allow us to effectively integrate the main findings of our studies. This "new" model can be seen in *Figure 12*. In addition, *figure 13* illustrates the main contributions from our nine studies. According to this model symptom patterns signify final frequent pathways resulting from the interaction of predisposing **(Stage 1),** precipitating (triggering) and maintaining **(Stage 2)** factors.

9.4.1. STAGE ONE: Predisposing factors

Stage one primarily examines factors that lead to the behavioural precursors of a disorder. Many of the predisposing factors in this stage are fixed markers (e.g. gender, age, etc), however psychosocial conditions also have a strong effect. At this point there is already a focus on the pre "illness" (prodromal) behavioural phenotype. Furthermore interactions within the family, the broader environment and genetics may already be present and may make a person susceptible to move further along the spectrum of development of pathology to the ED. Important predisposing factors include (a) genetics; (b) individual factors (e.g. personality and coping styles) and (c) family factors.

9.4.2. STAGE TWO: Precipitating/Maintaining factors

The primary goal of *stage two* is to assess what other precipitating factors combine and interact with a range of identified ED risk factors, which consecutively might trigger the development into an ED. The sparse quantity of existing research on this second phase is restricted in that any potential contributing factors have not been evidently acknowledged in the literature. Furthermore this stage also comprises a network of inter-related behavioural, cognitive and interpersonal mechanisms which might account for the persistence of EDs. The behavioural components of this stage generally comprise one or various of the following behaviours: dieting, bingeing, purging, exercise and/or starvation. Additionally, in the great majority of cases there is a central cognitive disturbance characterized by the over evaluation of eating, shape and weight and their control. Finally maladaptive interpersonal interactions such as high expressed emotion and enabling and accommodating behaviours may also serve to trigger and perpetuate the disorder (Schmidt & Treasure, 2006) In our model precipitating/maintaining factors include: (a) emotional disturbance; (b) negative attitudes towards life (c) non-ED related general psychopathology; (d) abnormal eating behaviour and (d) behavioural and cognitive ED symptoms.

9.4.3. Problems with the proposed model

The present model inherits some limitations which should be acknowledged. Many risk factors do not fit into a simple paradigm as a predisposing, precipitating, or maintaining factor and the precise mechanism of action for many known risks remains elusive. The period of vulnerability for certain risk factors is fixed because of their nature (e.g., gender or birth complications) whereas others may exert their influence at multiple points in the development and maintenance of the disorder (e.g., stressors, life events, expression of known and unkown genes). Furthermore, some factors can serve as risk and protective factors for disordered eating behaviour, depending on the processes of risk, the age of the individual at which the factor is working, etc. (Kraemer, Stice, Kazdin, Offord, & Kupfer, 2001). There is also an interdependence of risk factors with mediating and moderating mechanisms poorly understood to date (Kraemer et al., 2001). Finally, it should be noted that we have not proposed that these additional mechanisms necessarily operate simultaneously, nor have we suggested that they are active in every case. Indeed, their partial independence may account in part for the varied and fluid form of these disorders.

Figure 13: *An Etiopathological Model of Eating Disorders*

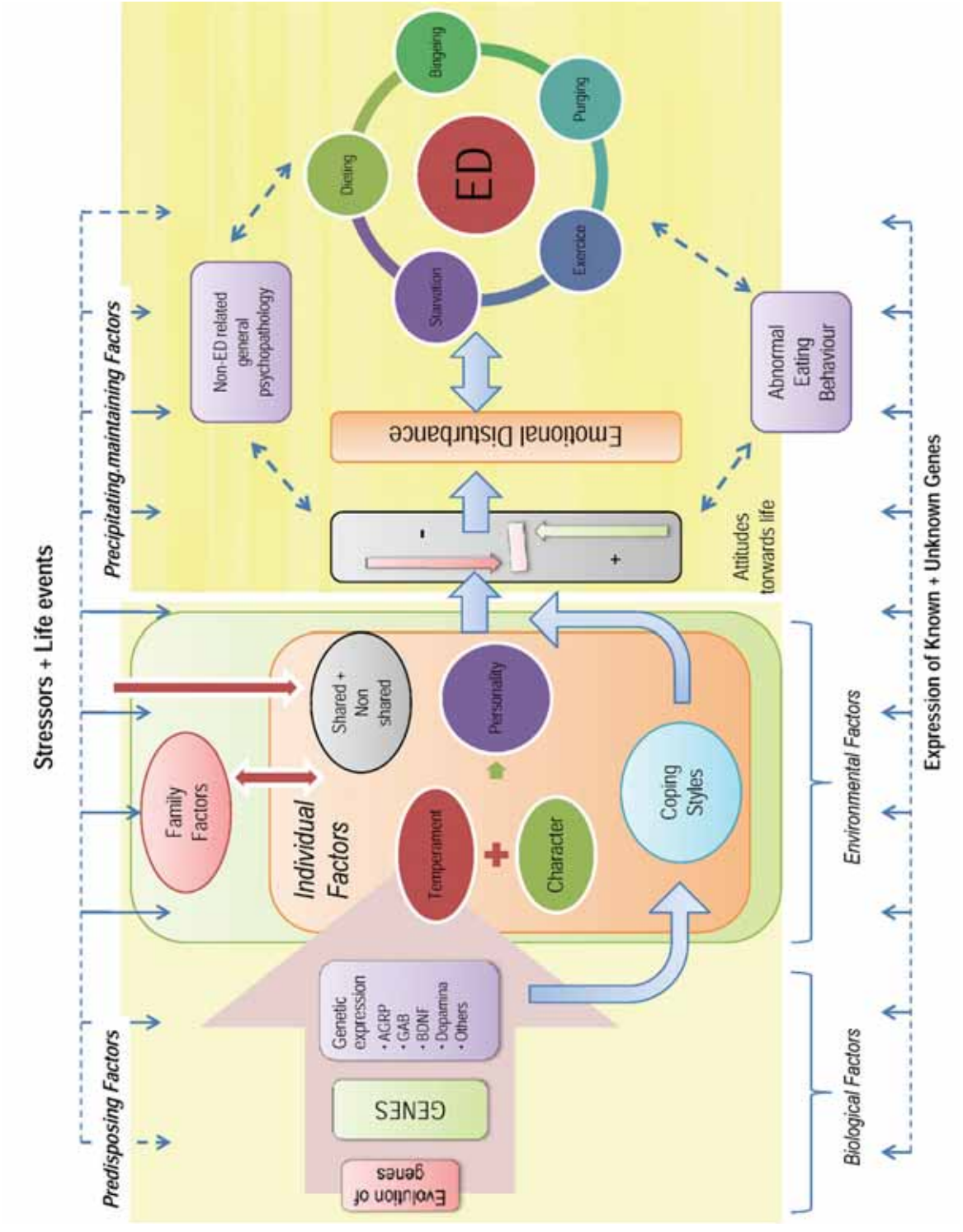
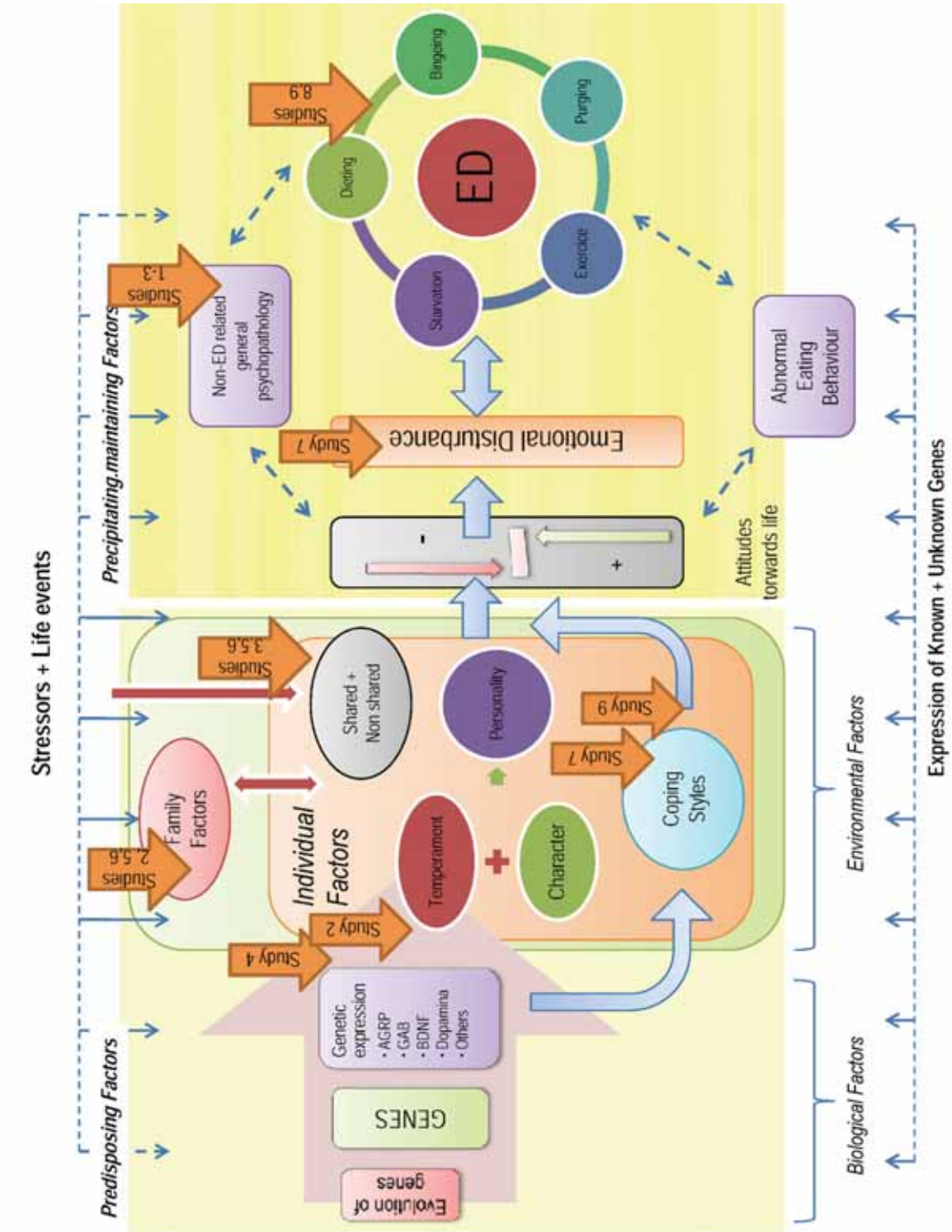


Figure 14: *Our Contributions to the Etiopathological Model of Eating Disorders*



9.5. Limitations of our studies

The results of our studies should be considered within the context of several limitations. First, the retrospective and self-report data collection procedures, may have limited the validity and the reliability of our findings. Second, the cross-sectional design does not allow us to determine causality of the variables assessed. Thirdly, our research used clinical samples of ED patients. This type of selection bias may offer insights only into a subpopulation of ED individuals but not necessarily capture the true nature of EDs. Fourthly, spurious results due to comorbidity of index patients with Axis I and Axis II diagnosis could not be quantified. Finally, since we did not account for a lifetime ED in some of the control samples **(e.g. Study 7)**, we cannot rule out that some controls may have had ED symptoms. On the other hand, this represents a more realistic and natural control group and a conservative bias.

9.6. Strengths of the present thesis

Notwithstanding these limitations, the present thesis entails highly ground-breaking research intended at generating an integrated etiological model of EDs. We were able to undertake mixed basic **(Study 4)** and psychological research and to assess numerous factors associated with EDs in a standard way in mostly large and phenotypically well-characterized samples of individuals with EDs. Previous studies have hardly relied on such a large sample. Furthermore, we were able to determine whether associated ED factors varied across countries in our two European Multicenter studies (**Studies 3 and 6)**, due to the large sample size across the countries.

9.7. Implications for treatment and prevention of eating disorders

Understanding more about how problematic eating patterns and substance use co-occur has important implications for assessment and treatment. Our first three studies **(Studies 1 to 3)** emphasize the importance of assessing substance use in individuals with disturbed eating behaviour, and vice versa and that treatment focused on both problems should be given conjointly.

From the mechanisms proposed in our animal study **(Study 4)**, the introduction of a regular eating pattern could reduce fasting periods and therefore extinguish the association between contextual cues and a long fasting period. Moreover, if places where patients had never eaten previously provide inhibitory properties, then the introduction of regular eating patterns in different contexts could extinguish or counter-condition this inhibitory conditioning.

Our findings from our individual and family eating pattern studies **(Studies 5 and 6)** suggest that if programs to improve childhood and adolescent eating patterns are to be successful, they need to focus on a wide range of environmental factors. In particular, the family should be informed about the importance of structuring meal times with shared meals and increasing the accessibility and promotion of snacks. Furthermore, maintaining structured family meals might encourage healthier diets in youngsters and could also allow the family to gain a better understanding of the child's food choices.

The results from **Study 7** highlight the importance of assisting patients in replacing emotion-focused coping strategies with a more adaptive problem-focused approach, whereby the anger can be directed adaptively to change the environment in such a way that the anger is no longer necessary or incapable of expression.

Ultimately, our last two studies **(Studies 8 and 9)** highlight the effectiveness of various forms of interventions (psychoeducation and non-symptom oriented CBT treatment). Furthermore, the results from **Study 9** indicate that treatment should always be tailored to the different facets of the patient´s characteristics and personal needs.

9.8. Future studies on eating disorders

The chief methods for examining mechanisms for all the factors we have assessed in the previously mentioned studies are prospective longitudinal studies of the stability, order of onset and course of the ED and co-morbid disorders.

Furthermore treatment studies that discriminate differential treatment response by patterns of these factors, and family and twin studies which examine whether these factors are attributable to common familial or genetic factors are required.

As regards to our substance use studies (**Studies 1 to 3**), further research should examine reports of substance use, characterizing such use in terms of its frequency, severity, quantity, consequences of, and attitudes toward the various disordered eating and substance use behaviours.

In relation to our animal study **(Study 4)** forthcoming research could assess pre-screened behavioural characteristics of animals that exhibit extreme phenotypes in the specific animal models (e.g., bingeing behaviour), which could lead to a list of predictive behavioural characteristics for EDs.

Upcoming research on individual and family eating patterns **(Studies 5 and 6)** should include further mediating factors, such as gender and age of the child, gender of the parent, type and severity of the ED or dieting behaviour, personality traits or cognitive style of the parent, and the temperament and appetite of the child.

As regards to our anger study **(Study 7)**, future studies should continue assessing anger as a multifaceted phenomenon and try to detect the presence and pervasiveness of anger, in order to provide adequate treatment.

Finally, the results of our treatment studies of EDs **(Studies 8 and 9)**, highlight the need for assessing treatment in atypical patients since virtually nothing is known about the treatment response of these patients. Furthermore, our comparison study of full and subthreshold BN **(Study 8)** indicates that further work is needed in attempting to split samples of individuals with EDNOS into meaningful groups. Ideally, such a study might employ empirical techniques such as latent structure analysis or taxometric analysis to a large sample, diverse in demography, behaviour, psychopathology and personality.

10. SUMMARY OF MAIN FINDINGS AND CONCLUSIONS

10.1. English

The central scientific objective of this thesis was to take a broad multidisciplinary approach to make use of the full potential information to battle EDs, utilizing an interactive and translational approach running from basic science through to the clinic. In our studies we assessed a.) clinical factors and comorbidity [namely substance use in EDs **(Studies 1 to 3)**], b.) psychosocial, behavioural and environmental correlates of EDs **(Studies 4 to 7)** and c.) treatment effectiveness of specific forms of ED interventions **(Studies 8 to 9)**.

Our first line of investigation comprised **Studies 1 to 3** and assessed the comorbidity of substance use in EDs. The results of these studies suggest that compared to healthy controls, substance use was higher in individuals with EDs **(Studies 1 and 3)**, that the presence of a family history of alcohol dependence was associated with the comorbidity of EDs and substance use **(Study 2)** that substance use was particularly prevalent in patients with bulimic characteristics **(Studies 1 to 3)** and that EDs and substance abuse may represent expressions of a fundamental predisposition to addictive behaviour possibly related to the genetically influenced traits such as novelty seeking **(Study 2)**. Furthermore, we revealed some significant differences for the specific forms of drugs in people with EDs **(Studies 1 and 3)**, which emphasize the significance of assessing various drug types in EDs. Finally we also observed cross-cultural differences across various European countries in the prevalence of substance use in EDs and healthy controls **(Study 3)**.

The second research area was labelled psychological, behavioural and environmental correlates of EDs. In our animal study **(Study 4)** we found that contextual conditioning of eating response was more effective when high than low density caloric food was used. This result indicates that animal models are

useful for analyzing and identifying human-animal links in feeding related behaviours.

Studies 5 and 6 assessed which early individual and family eating patterns play a role in the development of EDs. Our findings agree with the growing body of research indicating that a variety of environmental and social factors are associated with dysfunctional individual and family eating patterns (e.g. food used as individualization, control and rules about food) during the first years of life and which if not detected on time could lead to a subsequent ED. Conversely, healthy eating (including eating breakfast) was negatively linked to the development of a subsequent ED. Only a few differences across ED subtypes were observed. Finally some cross-cultural differences also emerged **(Study 6)**.

In **Study 7** we compared anger expressions in individuals with EDs and healthy controls and explored the relation among ED symptoms, comorbid psychopathology, personality traits and impulsive behaviours. The results indicated that individuals with EDs obtained significantly higher scores than controls on maladaptive anger expressions. When different purging methods were assessed independently, the frequency of laxative use was associated with anger suppression. ED symptoms and specific personality traits were also positively associated to different anger expressions. At last, we observed that inappropriate anger expressions were related to self-harming behaviours.

Finally our last research line assessed the effectiveness of various treatments for EDs. In **Study 8** we compared full and subthreshold BN in terms of personality, clinical characteristics and short-term response to a psychoeducational therapy. The results showed that full-BN and sub-BN share common psychopathological symptoms and personality traits. Furthermore, no differences in therapy outcome were observed in terms of general ED symptomatology and psychopathology. In **Study 9** we described and assessed a non-symptom oriented CBT treatment in a congenitally blind women. A dramatic reduction in ED symptoms was observed after the maintaining and triggering factors had been reduced.

To conclude, relatively little research has been performed towards understanding the aetiology of EDs. The findings from our investigations represent a major enhancement in the state of the art of EDs, and lead to the development of a new overall etiological model of EDs. The model we propose is a general understanding of how various ED predisposing and precipitating factors might eventually lead to EDs, and maintain the course of a disorder. Future work should address the effects of genes, environment and gene-environment interaction on the development and maintenance of EDs. Of specific interest is the query of which of these factors are non-specifically related to mental disorders and which factors may be more explicit factors that predispose an individual to EDs and related states, but not to mental disorders in general. The answers to these questions should hopefully become perceptible in the next couple of years.

10.2. Español

El objetivo principal de esta tesis ha sido el abordar los Trastornos de la alimentación (TCA) desde una aproximación multidisciplinar, que nos ayude a combatir los TCA desde una perspectiva traslacional, en la que confluyan investigaciones básicas y aplicadas. En nuestros estudios hemos analizado en profundidad los siguientes aspectos: a.) Factores clínicos y comorbilidad [especialmente abuso de sustancias en TCA] **(Estudios 1 a 3);** b.) Correlatos psicosociales, conductuales y ambientales en TCA **(Estudios 4 a 7)**; y c.) Eficacia de tratamientos específicos en TCA **(Estudios 8 a 9)**.

Nuestra primera línea de investigación (**Estudios 1-3**), ha estudiado la comorbilidad de abuso de sustancias en TCA. Los resultados de estos estudios sugieren que: a) abuso de sustancias es más prevalente en TCA que en sujetos de control **(Estudios 1 y 3)**; b) la presencia abuso de sustancias en pacientes con TCA, está asociada a historia familiar previa de dependencia de alcohol **(Estudio 2);** c) abuso de sustancias es especialmente prevalente en pacientes con características bulímicas **(Estudios 1 a 3)**; y d) que presencia de abuso de sustancias en TCA puede ser expresión de una predisposición a conductas adictivas, cuya susceptibilidad viene determinada por rasgos de personalidad

específicos (búsqueda de sensaciones) **(Estudio 2)**. Asimismo, encontramos aspectos diferenciales en TCA, en base al tipo de droga que consumen **(Estudio 1 y 3)**, hecho que enfatiza la importancia de evaluar los distintos tipos de drogas utilizados por estos pacientes. Finalmente, encontramos diferencias culturales entre distintos países europeos, respecto a la prevalencia de abuso de sustancias en TCA, al ser comparados con grupos de control **(estudio 3)**.

Como segunda área de investigación, nos centramos en aspectos psicológicos, conductuales y ambientales en TCA. En un estudio, realizado siguiendo un modelo animal **(estudio 4)**, encontramos que el condicionamiento contextual de respuesta alimentaria es más efectivo cuando es utilizado un alimento con alta densidad calórica, que cuando se utiliza un alimento con baja densidad calórica. Estos resultados sugieren qué modelos animales son útiles a la hora de analizar e identificar asociaciones entre comportamiento en humanos y animales, respecto a su conducta alimentaria.

En los **estudios 5 y 6** se analizaron en qué medida conductas alimentarias tempranas y patrones alimentarios en la familia, influyen en la aparición posterior de un TCA. Los resultados de estos estudios sugieren, en concordancia con un creciente volumen estudios recientes, la influencia que poseen aspectos ambientales y sociales en el desarrollo posterior de una conducta alimentaria anormal (p.e., control y reglas entorno a la alimentación). Por contrario, patrones alimentarios regulares (p.e., desayunar antes de ir al colegio) se encontró negativamente asociado (factor protector) a subsecuente desarrollo de un TCA. Asimismo, fueron encontradas limitadas diferencias entre subtipos diagnósticos, aunque algunas hacían referencia al contexto cultural **(estudio 6)**.

En el **estudio 7** comparamos la expresión de ira en sujetos con un TCA y un grupo control, y analizamos su asociación con sintomatología alimentaria, psicopatología general comórbida, rasgos de personalidad y conductas impulsivas. Nuestros resultados indicaron que pacientes con TCA manifestaban sentimientos de ira de forma más inadecuada que grupos control. Al analizar los

distintos procedimientos de purga, la frecuencia de abuso de laxantes iba asociada a supresión de sentimientos de ira.

La sintomatología alimentaria y algunos rasgos de personalidad se asociaban a determinadas formas inadecuadas de expresión de sentimientos. Asimismo, observamos que una inadecuada expresión de sentimientos en TCA se asociaba con una mayor frecuencia de conductas autoagresivas.

Finalmente, en nuestra última línea de investigación, analizamos la eficacia de distintos tipos de tratamiento en TCA. En el **estudio 8** comparamos casos totales y parciales de Bulimia nerviosa, en base rasgos de personalidad, sintomáticas alimentaria, psicopatología general y respuesta a un tratamiento de carácter psicoeducativo. Los resultados indicaron que los casos totales y parciales de BN comparten similitudes sintomáticas, psicopatológicas y de personalidad. Asimismo, no se obtuvieron diferencias respecto a la respuesta al tratamiento entre ambos grupos de pacientes. En el **estudio 9,** describimos y evaluamos un tratamiento cognitivo-conductual no centrado en los síntomas alimentarios, en una paciente ciega. En este caso, fue constatada una drástica reducción de los síntomas alimentarios tras este tipo de tratamiento.

En conclusión, hasta el momento, existen escasas referencias en la literatura que sirvan para esclarecer los aspectos etiopatológicos implicados en TCA. Los resultados obtenidos en nuestras investigaciones ayudan sobre el conocimiento actual de TCA, y contribuyen al desarrollo de un nuevo modelo multimodal de entendimiento de éstos. El modelo que proponemos combina la interacción de diversos factores (predisponentes, precipitantes y mantenedores). Trabajos futuros deberían prestar atención a la relevancia que tienen factores genéticos, ambientales e interacción genes-ambiente, en el desarrollo y mantenimiento de los TCA. Un especial interés presenta la pregunta de cuáles de estos factores son específicos para trastornos mentales y cuáles los son para TCA de forma específica.

10.3. Català

L'objectiu principal d'aquesta tesi ha estat l'abordar els Trastorns de la conducta alimentària (TCA) des d'una aproximació multidisciplinar, que ens ajudi a combatre'ls des d'una perspectiva traslacional, en la que conflueixin investigacions bàsiques i aplicades. En els nostres estudis hem analitzat en profunditat els següents aspectes: a.) Factors clínics i comorbilitat [especialment abús de substàncies en TCA] **(Estudis 1 a 3)**; b.) Correlats psicosocials, conductuals i ambientals en TCA **(Estudis 4 a 7)**; i c.) Eficàcia de tractaments específics en TCA **(Estudis 8 a 9)**.

La nostra primera línia d'investigació **(Estudis 1 a 3)**, ha estudiat la comorbilitat d'abús de substàncies en TCA. Els resultats d'aquests estudis suggereixen que: a) l'abús de substàncies és més prevalent en TCA que en subjectes control **(Estudis 1 i 3)**; b) la presència d'abús de substàncies en pacients amb TCA, està associada a història familiar prèvia de dependència d'alcohol **(Estudi 2)**; c) l'abús de substàncies és especialment prevalent en pacients amb característiques bulímiques **(Estudis 1 a 3)**; i d) que la presència d'abús de substàncies en TCA pot ser expressió d'una predisposició a conductes addictives, la susceptibilitat de les quals ve determinada per trets de personalitat específics (recerca percaça de sensacions) **(Estudi 2)**. Així mateix, trobem aspectes diferencials en TCA, en base al tipus de droga que consumeixen **(Estudis 1 i 3)**, fet que emfatitza la importància d'avaluar els diferents tipus de drogues utilitzats per aquests pacients. Finalment trobem diferències culturals entre distints països europeus, respecte a la prevalença d'abús de substàncies en TCA, al ser comparats amb grups control **(Estudi 3)**.

Com a segona àrea d'investigació, ens centrem en aspectes psicològics, conductuals i ambientals en TCA. En un estudi realitzat seguint un model animal **(Estudi 4)**, trobem que el condicionament contextual de resposta alimentària és més efectiu quan s'utilitza un aliment amb alta densitat calòrica, que quan se'n utilitza un amb baixa densitat calòrica. Aquests resultats suggereixen que els models animals són útils a l'hora d'analitzar i identificar

associacions entre comportament en humans i animals, respecte la seva conducta alimentària.

En els **estudis 5 i 6** es varen analitzar fins a quin punt conductes alimentàries primerenques i patrons alimentaris en la família influeixen en l'aparició posterior d'un TCA. Els resultats d'aquests estudis suggereixen, en concordància amb un volum creixent d'estudis recents, la influència que tenen aspectes ambientals i socials en el desenvolupament posterior d'una conducta alimentària anormal (per exemple, control i normes entorn a l'alimentació). Tanmateix, patrons alimentaris regulars (per exemple, esmorzar abans d'anar a l'escola) estaven negativament associats (factor protector) al subseqüent desenvolupament d'un TCA. Així mateix, es varen trobar diferències limitades entre subtipus diagnòstics. Finalment, es varen trobar algunes diferències en relació al context sociocultural. **(Estudi 6).**

En l'**estudi 7** vàrem comparar expressió d'ira en subjectes amb un TCA i un grup control, i vàrem analitzar la seva associació amb simptomatologia alimentària, psicopatologia general comòrbida, trets de personalitat i conductes impulsives. Els nostres resultats varen indicar que pacients amb TCA manifestaven sentiments d'ira de forma més inadequada que grups control. A l'analitzar els diferents procediments de purga, la freqüència d'abús de laxants anava associada a la supressió de sentiments d'ira.

La simptomatologia alimentària i determinats trets de personalitat, s'associaven a determinades formes inadequades d'expressió de sentiments. Així mateix, vàrem observar que una expressió inadequada de sentiments en TCA anava associada a una freqüència major de conductes autoagressives.

Finalment, en la nostra darrera línia d'investigació vàrem analitzar l'eficàcia de diferents tipus de tractament en TCA. En l'**estudi 8** vàrem comparar casos totals i parcials de Bulímia nerviosa (BN), en base a trets de personalitat,

simptomatologia alimentària, psicopatologia general i resposta a un tractament de caràcter psicoeducatiu. Els resultats varen indicar que els casos totals i parcials de BN, comparteixen similituds simptomatològiques, psicopatològiques i de personalitat. Així mateix, no es varen obtenir diferències respecte a la resposta del tractament entre ambdós grups de pacients. En l'**estudi 9**, vàrem descriure i avaluar un tractament cognitiu-conductual no centrat en els símptomes alimentaris, en una pacient cega. En aquest cas es va constatar una reducció dràstica dels símptomes alimentaris després d'aquest tipus de tractament.

Fins el moment, existeixen escasses referències en la literatura que serveixin per aclarir els aspectes etiopatogènics implicats en els TCAs. Els resultats obtinguts en les nostres investigacions ajuden en el coneixement actual dels TCA i contribueixen al desenvolupament d'un nou model multimodal per la comprensió de la seva etiologia. El model que proposem combina la interacció de diversos factors (predisponents, precipitants i mantenidors). Els treballs futurs haurien de incidir en la rellevància que tenen els factors genètics, ambientals i la interacció d'ambdós, en el desenvolupament i manteniment dels TCA. És d'especial interès la qüestió de quins d'aquests factors són específics per trastorns mentals i quins ho són per TCA.

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APPENDIX I: CURRICULUM VITA

CURRICULUM VITA

PERSONAL DETAILS

Name: **Isabel Krug**
Work Address: Hospital Universitario de Bellvitge
Feixa Llarga s/n,
L`Hospitalet del ´Llobregat,
08907
E-mail: ikrug@csub.scs.es
Date of birth: December 27th, 1980
Place of birth: Casablanca, Morocco
Nationality: Austrian

CURRENT POSITION

- Research Member CIBER (Fisiopatología Obesidad y Nutrición), Instituto Carlos III, excellence Research Network of Spanish Ministerio de Sanidad.

- Researcher and studentship for predoctoral studies from the Catalan government (2005 FI 00425)- 2005-2008. Eating Disorders Unit (Head Dr. Fernando Fernández-Aranda), Dept. of Psychiatry, University Hospital of Bellvitge

EDUCATION

Present- 2005	**University Autonoma of Barcelona, Spain**
	Postgraduate Degree in Advanced Statistics
Present -2003	**University of Barcelona, Spain**
	Master in Psychotherapy
2003-2008	**University of Barcelona, Spain (expected October 2008)**
	PhD in Clinical and Health Psychology
2003-2005	**University of Barcelona, Spain**
	DEA (Diploma de Estudios Avanzados)
	MSc in Advanced Research Methods
2002 – 2003	**University College London, UK**
	MSc in Health Psychology
	University of Cardiff, Wales, UK
	BSc in Psychology
1997 - 1999	**Frankfurt International School, Germany**
	International Baccalaureate and High School Diploma
1992 - 1997	**Istanbul Alman Lisesi, Turkey** (High School)
1988 - 1992	**Deutsche Botschaftsschule Istanbul, Turkey** (Primary School)
1987 - 1988	**Theodor Heuss Schule, Germany** (Primary School)

CLINICAL TRAINING

Present- 04/2004	**Predoctoral Researcher and Clinical training** at the Eating Disorders Unit (Head Dr. Fernando Fernández-Aranda), Dept. of Psychiatry, University Hospital of Bellvitge, Barcelona.
2006 - 01/2004	**Clinical training in various recognized mental health institutions in Barcelona, Spain.**

Association Septimania; Manso; School of Family Therapy, Hospital of Santa Creu and Sant Pau.

09/2001 – 2002 **Whitchurch Project, Psychiatric Hospital in Cardiff, UK**

(Student volunteering in the community) Involved in visiting patients suffering from a variety of mental health problems.

09/2001 – 2002 **Connect Project, University of Cardiff, UK**

(Student volunteering in the community) Involved in working with children who are within the autistic spectrum.

06/2001 – 08/2001 **Psychosomatic Station, University Clinic of Ulm, Germany**

(Internship for Psychological studies) Participation in department meetings, doctor visits, supervisions, art and music therapies, responsible for the care of several patients, substituting

TEACHING ACTIVITIES

1.) Lecturer: Master de Psicología Clínica en Hospitals Generals. (2005-2007), IL3, Universisat de Barcelona (Director: Dra. Susana Jiménez-Murcia)

2.) Lecturer: Societat Catalana de Recerca i Terapia del Comportament (SCRITC). (2007). Cursos trastornos de la conducta alimentaria. Evaluacion Psicologica y neuropsicologica. (Course in Eating Disorders: Psychological and neuropsychological evaluation), Hopsital del Bellvitge, Barcelona, 23-31 March.

PUBLICATIONS

1.) Fernández-Aranda, F., Casanovas, C., Jiménez -Murcia, S., **Krug, I.,** Martinez, C., Nunez, A., Ramos, M.J., Sanchez, I., & Vallejo, J. (2004). Eficacia del tratamiento ambulatorio en bulímia nervosa. Revista Psicologia Conductual, 12 (3): 501-518.

2.) Fernández-Aranda, F., Crepso, J.M., Jiménez-Murcia, S., **Krug, I.,** & Vallejo, J. (2006). Blindness and bulimia nervosa: A description of a case-report and its treatment. International Journal of Eating Disorders, 39, 263-265

3.) Fernandez-Aranda, F., Jimenez-Murcia, S., Bulik, C.M., **Krug. I.,** Forcano, L., Alvarez-Moya, E.M. (2006). Terapia grupal en trastornos de la alimentación. Aula Medica Psiquiatria, 3, 123-142.

4.) Fernández-Aranda, F., **Krug, I.,** Ramon, J.M., Badia, A., Jiménez, L., Solano, R., Vallejo, J., Collier, D., Karawautz, A., & Treasure, J. (2007). Childhood eating patterns and paternal attitudes to food: an analysis of risk factors in eating disorders. Appetite, Sep; 49 (2): 476-85.

5.) Jiménez -Murcia, S., Fernández-Aranda, F., Raich, R.M., Alonso, P., **Krug, I.,** Jaurrieta, N., Alvarez-Moya, E., Labad, J., Menchon, J.M., & Vallejo, J. (2007). Obsessive-compulsive and eating disorders: comparison of clinical and personality features. Psychiatry Clin Neurosci, Aug; 61(4): 385-91.

6.) Casasnovas, C., Fernández-Aranda, F., Granero, R., **Krug, I.,** & Vallejo, J. (2007) Stage of Change in anorexia and bulimia nervosa. Clinical and therapeutical implications. European Eating Disorders Review, Nov;15(6), 449-56.

7.) Álvarez-Moya, E.M.; Jiménez-Murcia, S.; Granero, R.; Vallejo, J.; **Krug, I.**; Bulik, C.M.; Fernández-Aranda, F. (2007). Comparison of personality risk factors in Bulimia nervosa and Pathological gambling. Comprehensive Psychiatry, 48, 452– 457.

8.) Krug, I., Casasnovas, C., Martinez, C., Jimenez-Murcia, Bulik, C.M., Roser, G., & Fernández-Aranda, F. (2008) Brief-psychoeducational therapy for EDNOS: a short-term effectiveness comparison study. Psychotherapy Research,18 (1), 37 – 47.

9.) Krug I., Treasure, J., Anderluh, M., Bellodi, L., Cellini, E., di Bernardo, M., Karwautz, A., Nacmias, B., Ricca ,V., Sorbi, S., Tchanturia, K., Wagner, G., Collier, D., & Fernandez-Aranda, F. (in press). Present and lifetime comorbidity of tobacco, alcohol and drug use in eating disorders: A European Multicenter study. Drug and Alcohol Dependence.

10.) Sansa, J., **Krug, I.,** Chamizo, V.D., & Fernandez-Aranda, F. (in press). An animal model of learning in binge eating: the role of cotnextual conditioning and food density. Psicologica: International Journal of Methodology and Experimental Psychology.

11.) Krug, I., Bulik, C.M., Nebot Vall-Llovera, O., Granero, R., Agüera, Z., Villarejo, C., Jiménez, S., & Fernández-Aranda, F. (In press). Anger expression in eating disorders: clinical, psychopathological and personality correlates. Psychiatry Research (doi: 10.1080/ 10503300701320652).

12.) Forcano, L., Santamaría, J., Agüera, Z., Gunnard, K., Tchanturia, K., **Krug, I.,** Treasure, J., Granero, R., Penelo, E., Jiménez-Murcia, S., & Fernández-Aranda, F (In press). First generation Latin-American immigrants vs. Spanish native-born bulimia nervosa patients: clinical and therapeutic implications. International Journal of Child and Adolescent Health.

13.) Fernández-Aranda, F., Núñez, A., Martínez, C., **Krug, I.,** Cappozo, M., Carrard, I., Royget, P., Jimenez-Murcia, S., Granero, R., Penelo, E., Santamaria, J., & Lam, T. (In press). New Technologies for the therapy of Bulimia nervosa. CyberPsychology and Behavior.

14.) Krug, I., Treasure, J., Anderluh, M., Bellodi, L., Cellini, E., Collier, D., Karwautz, A., Nacmias, B., Granero, R., Sorbi, S., Tchanturia, K., Wagner, G., & Fernández-Aranda, F. (2008). Association of childhood eating patterns and parental attitudes to food in eating disorders: A multicenter study. British Journal of Nutrition (doi:1017/S000711450804775).

15.) Fernández-Aranda, F., **Krug, I.,** Jimenez-Murcia, S., Granero, R., Nunez, A., Penelo, E., Solano, R., & Treasure, J. (In press). Male eating disorders and therapy: A Pilot Study. Journal of Behavior Therapy and Experimental Psychiatry

16.) Krug, I., Poyastro Pinheiro, A., Bulik, C., Jiménez-Murcia, S., Granero, R., Penelo, E., Masuet, C., Aguera, Z., & Fernández-Aranda, F. (In press). Lifetime substance abuse, family history of alcohol dependence and novelty seeking in eating disorders: A comparison study of eating disorders subgroups. .Psychiatry and Clinical Neurosciences.

17.) Forcano, L., Fernandez-Aranda, F., Santamaria, J., Jimenez-Murcia, S., Granero, R., Krug, I., Riesco, N., Alvarez, E., & Bulik, CM. (In press). Suicidal behavior and ideation in bulimia nervosa. European Psychiatry

18.) Calero, A., **Krug, I.,** Davis, K., Lopez, C., Fernandez-Aranda, F., & Treasure, J. (Submitted). Meta-Analysis on drugs in people with eating disorders.

19.) Penelo, E., Granero R., **Krug, I.,** Treasure, J., Anderluh, M., Bellodi, L., Cellini, E., di Bernardo, M., Karwautz, A., Nacmias, B., Ricca, V., Sorbi, S., Tchanturia, K., Wagner, G., Collier, D., Bonillo, A., & Fernandez-Aranda, F. (Submitted). Validation of the Cross-Cultural (Enviornmental) Questionnaire-CCQ-in the context of the ED Framework V European Project.

20.) Nunez- Navarro, A., Villarejo, C., Alvarez-Moya, E., Bueno, B., Jimenez- Murcia, S., Granero, R., **Krug, I.,** Tinahones., Bulik, C., & Fernandez-Aranda, F. (Submitted). Bulimia Nervosa Vs. Binge Eating Disorder: Common and differential clinical and personality correlates.

PARTICIPATION IN CONGRESSES

1.) POSTERS

a.) NATIONALS

1.) Casasnovas, C., Badía,A., Solano,R., **Krug, I.**, & Fernández-Aranda, F. (2004). Motivación hacia el cambio en trastornos de la conducta alimentaria: implicaciones clínicas y terapéuticas. XIX Jornada Anual de la Societat Catalana de Recerca i Terapia del Comportament (SCRITC), 7 Mayo.

2.) Sansa, J., **Krug, I.,** Chamizo, V.D., & Fernández-Aranda, F. (2005). An Animal Model of Learning in Binge Eating: The Role of Contextual Conditioning and Density of Food. XVII Congreso de la Sociedad Española de Psicologia Comparada. Reunion International, Madrid, 14-16 Septiembre.

3.) Krug, I., Bellodi, L., Breceli, J., Collier, D., Karwautz,A., Nacmias, B., Roser, G., Tchanturia, K., Treasure, J., Wagner, G., Fernandez-Aranda, F. Associacion entre habitos alimentarios durante la infancia y actitudes parentales respecto a la alimentacion: un estudio europeo multicentrico. Congreso Hispano Latinomareicano de Trastornos de la Conducta Alimentaria, Barcelona, 6 de junio 2006.

4.) Sansa, J., **Krug, I.,** Chamizo, V.D., Fernandez-Aranda, F. Un modelo de aprendizaje con animales de la conducta de atracon: El papel del condicionamiento del contexto y densidad

energetica del alimento. Congreso Hispano Latinoamericano de Trastornos de la Conducta Alimentaria, Barcelona, 6 de junio 2006.

5.) Bonillo, A., Granero, R., **Krug, I.,** Anderluh, M., Belodi, L., Colier, D.A., Karwautz, A., Nacmias, B., Treasure, T., & Fernandez-Aranda, F. (2006). Fiabilidad y validez psicometrica del cuestionario transcultural CCRFQ a partit de un projecto multicentrico Europea. Congreso Hispano Latinoamericano de Trastornos de la Conducta Aliemntaria, Barcelona, 6 de junio 2006.

6.) Krug, I., Treasure, J., Adnerluh, M., Bellodi, L., Cellini, E., Collier, D., DiBernardo, M., Karwautz, A., Nacmias, B., Granero, R., Ricca, V., Sorbi, S., Tchanturia, K., Wagner, G., Fernandez-Aranda, F. (2007). Asociacion entre habitos alimentarios durante la infancia y actitudes parentales respecto a la alimentacion: un estidio europeo multicentrico. I Symposium Santiago de Compostela, Noviembre 22-24, Santiago, Spain

7.) Aguera, Z.P., Nunez-Navarro, A., **Krug, I.,** Jimenez-Murcia, S., Granero, R., Penelo, E., Karwautz, A., Collier, D., Treasure, J., Fernandez-Aranda, F. (2007). Rasgos psicopatologicos y de personalidad en una meustra espanola de varones con trastorno de la conducta alimentaria: estudio comparativo de casos y controles. I Symposium Santiago de Compostela, Noviembre 22-24, Santiago, Spain

8.) Villarejo, C., Nunez-Navarro, A., Alvarez-Moya, E.M., Bueno, B., Jimenez-Murcia, S., Granero, R., **Krug, I.,** Masuet, C., Tinahones, F., Bulik, C.M., & Fernandez-Aranda, F. (2007). Bulimia nervosa vs. Trastorno por atracon: diferencias y semejanzas clinicas de personalidad. I Symposium Santiago de Compostela, Noviembre 22-24, Santiago, Spain

b.) INTERNATIONALS

9.) Fernández-Aranda, F., Martinez, C., Nuñez, A., **Krug. I.,** Casanovas, C., & Vallejo, J. (2005). Brief-psychoeducational therapy for EDNOS: a short-term effectiveness comparison study. International Conference on Eating Disorders, Montreal, April 27-30th.

10.) Sansa, J., **Krug, I.,** Chamizo, V.D., & Fernández-Aranda, F. (2005). An animal model of learning in binge eating: The role of contextual conditioning and density of food. Research Society on Eating Disorders, Toronto, September, 2005.

11.) Casasnovas, C., Fernández-Aranda, F., Granero, R., **Krug, I.,** & Vallejo, J. (2005) Stage of change in anorexia and bulimia nervosa. Clinical and therpeutical implications. Research Society on Eating Disorders, Toronto, September 2005.

12.) Casasnovas, C., Fernandesz-Aranda, F., Granero, R., **Krug, I.,** & Vallejo, J. Stage of change in anorexia and bulimia nervosa. Clinical and therpeutical implications. International Conference on Eating Disorders, Barcelona, June 7-10th.

13.) Krug, I., Collier, D., Treasure, J., & Fernandez-Aranda, F. The impact of body image experiences during childhood and early adolescence on the development of eating disorders later in life. International Conference on Eating Disorders, Barcelona, June 7-10th.

14.) Krug, I., Bulik, C., Nebot, O., Granero, R., Aguirregabiria, B., Castro, Y., Fernandez-Aranda, F., (2006). Anger expression in eating disorders:clinical, psychopathological and personality correlates. Kongress Essstoerungen 2006, 19-21 October, Alpbach, Austria.

15.) Krug, I. (2006) Moderacion de sesion de posters: Obesity and Overweight (2006). Kongress Essstoerungen, 19-21, October, Alpbach, Austria

16.) Krug, I., Ogden, J., Holliday, J., Southgate, L., Fernandez-Aranda, F., & Treasure, J. (2007). The correlates of recovery from eating disorders:ristics, help-seeking behaviour, illness cognitions, social support and coping styles. International Conference on Eating Disorders, Baltimore, 2-5 May.

17.) Krug, I., Bulik, C., Nebot, O., Granero, R., Aguera, Z., Villarejo, C., Jimenez-Murcia, S., & Fernandez-Aranda, F., (2007). Anger expression in eating disorders:clinical, psychopathological and personality correlates. European Council on Eating Disorders, 19-21, September, Porto, Portugal

18.) Forcano, L., Santamaría, J., Jiménez-Murcia, S., Granero, R., **Krug, I.,** Riesco, N., Álvarez, E., Bulik, CM & Fernandez-Aranda, F. (2007) Suicidal behavior and ideation in bulimia nervosa. European Council on Eating Disorders, 19-21, September, Porto, Portugal

19.) Krug, I., Ogden, J., Holliday, J., Southgate, L., Fernandez-Aranda, F., & Treasure, J. (2007). The correlates of recovery from eating disorders:ristics, help-seeking behaviour,

illness cognitions, social support and coping styles. Kongress Essstoerungen, 18-20 Oktober, Alpbach, Tirol, Oesterreich / Austria.

20.) Krug, I., Treasure, J., Anderluh, M., Bellodi, L., Cellini, E., di Bernardo, M., Granero, R., Karwautz, A., Nacmias, B., Penelo, E., Ricca, V., Sorbi, S., Tchanturia, K., Wagner, G., Collier, D., & Fernandez-Aranda, F (2008). Comorbid alcohol and drug use in eating disorders: A Multicenter European study. Present and lifetime comorbidity of tobacco, alcohol and drug use in eating disorders: A Multicenter study. 16th European Congress of Psychiatry, Nice, France, April 5-9. Abstract published at the European Psychiatry (2008), 23-suppl. 2- S81-S191 (p. S183- P0346).

21.) Calero, A., **Krug, I.,** Davis, K., Lopez, C., Fernandez-Aranda, F., & Treasure, J. (2008). Meta-analysis on drugs in people with eating disorders. 16th European Congress of Psychiatry, Nice, France, April 5-9. Abstract published at the European Psychiatry (2008), 23-suppl. 2- S81-S191 (p. S184- P0348).

22.) Krug, I., Treasure, J., Anderluh, M., Bellodi, L., Cellini, E., Collier, D., di Bernardo, M., Granero, R., Karwautz, A., Nacmias, B., Penelo, E., Ricca, V., Sorbi, S., Tchanturia, K., Wagner, G., & Fernandez-Aranda, F (2008). Individual and family eating patterns during childhood and early adolescence: A multicenter European study of associated eating disordered factors. 16th European Congress of Psychiatry, Nice, France, April 5-9. Abstract published at the European Psychiatry (2008), 23-suppl. 2- S81-S191 (p. S183- P0347).

23.) Aguera, Z.P., Nunez-Navarro, A., **Krug, I.,** Jiménez-Murcia, S., Granero, R., Penelo, E., Karwautz, A., Collier, D., Treasure, J & Fernandez-Aranda, F. (2008). Personality and psychopathological traits in Spanish eating disordered males: A comparative study. 16th European Congress of Psychiatry, Nice, France, April 5-9. Abstract published at the European Psychiatry (2008), 23-suppl. 2- S81-S191 (p. S178- P0330).

24.) Forcano, L., Fernandez-Aranda, F., Alvarez-Moya, E.M., Bulik, C.M., Cariacedo, A., Granero, R., Gratacos, M., Jiménez-Murcia, S., **Krug, I.,** Mercader, J.M., Saus, E., Santamaría, J., & Estivill, X. (2008). Suicide attempts in bulimia nervosa: personality, psychopathological and genetic correlates. 16th European Congress of Psychiatry, Nice, France, April 5-9. Abstract published at the European Psychiatry (2008), 23-suppl. 2- S81-S191 (p. S181- P0339).

25.) Fernandez-Aranda, F., Santamaria, J., Nunez, A., Martinez, C., **Krug, I.,** Cappozzo, M., Carrard, I., & Rouget, P., Jiménez-Murcia, S., Granero, R., Penelo, E., & Lam, T. (2008).

Internet-based cognitive-behavioral therapy for bulimia nervosa: A controlled study. 16th European Congress of Psychiatry, Nice, France, April 5-9. Abstract published at the European Psychiatry (2008), 23-suppl. 2- S81-S191 (p. S186- P0355).

26.) Villarejo, C., Nunez-Navarro, A., Alvarez-Moya, E.M., Bueno, B., Jiménez-Murcia, S., Granero, R., **Krug, I.,** Masuet, C., Tinahones, F., Bulik, C.M., Fernandez-Arnada, F. (2008). Bulimia Nervosa vs. Binge eating disorder: common and differential clinical and personaliyt correlatos. 16th European Congress of Psychiatry, Nice, France, April 5-9. Abstract published at the European Psychiatry (2008), 23-suppl. 2- S81-S191 (p. S186- P0358).

27.) Jimenez-Murcia, S., Fernandez-Aranda, F., aich, R.M., Alonso, P., **Krug, I.,** Jaurrieta, N., Alvarez-Moya, E., Labad, J., Menchon, J.M., & Vallejo, J. (2008). Obsessive-Compulsive and eating disorders: a comparison of clinical and personality features. 16th European Congress of Psychiatry, Nice, France, April 5-9 .

28.) Krug, I., Pinheiro, AP., Bulik, CM., Jiménez-Murcia, S., Granero, R., Agüera, Z., Fernández-Aranda, F. (2008). Lifetime substance abuse, family history of alcohol dependence and novelty seeking in eating disorders: A comparison study of eating disorder subgroups. International Conference on Eating Disorders, May 14-17, Seattle, Washington, USA

2.) ORAL COMUNICATIONS

a.) NATIONALS

1.) Alvarez, E., Jimenez-Murcia,S., Granero, R., **Krug, I.,** Nunez, A., F., Forcano, L., Snachez, I., Fernandez-Aranda, A. (2006) Trastonros del control dels impulsos en trastornos de l'alimentacio: implicaciones cliniques i terapeutiques.XXI Jornada de terapia del comportament i medicina conductual en la practica clinica, 6 de Abril, Barcelona.

b.) INTERNATIONALES

2.) Fernández-Aranda, F., Badia, A., Solano, R., **Krug, I.,** & Vallejo, J. (2005) Brief Hospitalization plus outpatient group therapy in bulimia nervosa: analysis of the effectivness of a combined treatment. International Conference on Eating Disorders, Montreal, April 27-30th.

3.) Krug, I., Bellodi, L., Breceli, J., Collier, D., Karwautz, A., Nacmias, B., Roser, G., Tchanturia, K., Treasure, J., Wagner, G., & Fernandez-Aranda, F. Associations of childhood eating patterns and parental attitudes to food: A Multicenter European study. International Conference on Eating Disorders, Barcelona, June 7-10th.

4.) Sansa, J., **Krug, I.,** Chamizo, V.D., & Fernandez-Aranda, F. (2006). An animal model of learnign in binge eating: The role of contextual conditioning and density of food. International Conference on Eating Disorderes, Barcelona, June 7-10th, 2006

5.) Krug, I., Casanovas, C., Martinez, C., Jimenez-Murcia, Bulik, C.M., Roser, G., & Fernandez-Aranda, F. Brief-psychoeducational therapy for EDNOS: a short-term effectiveness comparison study. Kongress Essstoerungen 2006, 19-21 October, Alpbach, Austria.

6.) Fernández-Aranda, F., Forcano, L., Santamaría, J., Jiménez-Murcia, S., Granero, R., **Krug, I.,** Riesco, N., Álvarez, E., & Bulik, CM. Suicidal behavior and ideation in bulimia nervosa. International Conference on Eating Disorders. Baltimore, 2-5 May, 2007.

7.) Krug, I., Treasure, J., Anderluh, M., Bellodi, L., Cellini, E., di Bernardo, M., Karwautz, A., Nacmias, B., Ricca, V., Sorbi, S., Tchanturia, K., Wagner, G., Collier, D., & Fernandez-Aranda, F (2007). Comorbid alcohol and drug use in eating disorders: A Multicenter European study. European Council on Eating Disorders, 19-21, September, Porto, Portugal

8.) Krug, I., Treasure, J., Anderluh, M., Bellodi, L., Cellini, E., di Bernardo, M., Karwautz, A., Nacmias, B., Ricca, V., Sorbi, S., Tchanturia, K., Wagner, G., Collier, D., & Fernandez-Aranda, F (2007). Comorbid alcohol and drug use in eating disorders: A Multicenter European study. Kongress Essstoerungen, 18-20 Oktober, Alpbach, Tirol, Oesterreich / Austria.

9.) Krug, I., Forcano, L., Fernandez-Aranda, F., Santamaría, J., Jiménez-Murcia, S., Granero, R., Riesco, N., Álvarez, E., & Bulik, CM. Suicidal behavior and ideation in bulimia nervosa. Kongress Essstoerungen, 18-20 Oktober, Alpbach, Tirol, Oesterreich / Austria.

10.) Krug, I., Treasure, J., Anderluh, M., Bellodi, L., Cellini, E., di Bernardo, M., Karwautz, A., Nacmias, B., Ricca, V., Sorbi, S., Tchanturia, K., Wagner, G., Collier, D., & Fernandez-Aranda, F (2008). Lifetime comorbidity of tobacco, alcohol and drug use in eating disorders: A European Multicenter study. International Conference on Eating Disorders, May 14-17, Seattle, Washington, USA.

11.) Calero, A., **Krug, I.,** Davis, K., Lopez, C., Fernandez-Aranda, F., & Treasure, J. (2008). Meta-analysis on drugs in people with eating disorders. International Conference on Eating Disorders, May 14-17, Seattle, Washington, USA.

INVITED PLENARIES/WORKSHOPS/ POSTER PRESENTATIONS:

1.) Fernández-Aranda, F., Núñez, A., Martínez, C. & **Krug, I.** (2005). "Evaluation of the effectiveness of the Spanish version of the web-based self-help guide for bulimia nervosa: A controlled study". Meeting of the Society for Psychotherapy Research, Lausanne, March, 2-5.

2.) Russell, G., Arthur, C., van Elburg A., **Krug, I.,** & Wentz, E. (2005).A conversation with Arthur Crisp & Gerald Russell. (Special Session) European Council on Eating Disorders, Innsbruck, 7-9 September, Austria.

3.) Krug, I. (2006). Chair at Poster panel at the 14th International Congress on eating Disorders/ Netzwerk Essstoerungen: Obesity and Overweight Kongress Essstoerungen, 19-21, October, Alpbach, Austria

4.) Krug, I. (2007). Workshop on risk factors and treatment efficacy. Curriculum. Esstoerungen. Parkland-Klinik-Fachklinik fuer Psychosomatik und Psychotherapie, 6-9 June, Bad Wildungen-Reinhardshausen, Germany.

5.) Krug, I & Fernandez-Aranda, F. (2007). Invited lecture on PCASOE- Perfil clinico e eficacia de terapeuticas /TCANE- Perfil clinico y eficacia de tratamiento. Encontro Iberico de DCA, 18 September, Lisabon, Portugal.

6.) Krug, I. (2007). Chair at Poster panel at the 15th International Congress on Eating Disorders/ Netzwerk Essstoerungen: Therapie, Kongress Essstoerungen, 18-20 Oktober, Alpbach, Tirol, Oesterreich / Austria.

7.) Fernandez-Aranda, F., **Krug, I.,** Collier, D., Karwautz, A., Treasure, J., & " Healthy Eating Consortium". Developmental continuities in eating and nutrition. 16th European Congress of Psychiatry, Nice, France, April 5-9 2008

8.) Karwautz, A., Wagner, G., Waldherr, K., Fernandez-Aranda, F., Krug, I., Ribases, M., Holliday, J., Collier, D.A., & Treasure, J. Gene-environement interaction in anorexia nervosa. 16th European Congress of Psychiatry, Nice, France, April 5-9 2008

9.) Fernández-Aranda, F., Núñez, A., Martínez, C., **Krug, I.,** Cappozzo, M., Carrard, I., Rouget, P., Jiménez-Murcia, S., Granero, R., Penelo, E., & Lam, T. (2008). Internet based cognitive-behavioral therapy for bulimia nervosa: A controlled study 39th Annual Meeting Society for Psychotherapy Research, June 18-21, 2008, Barcelona, Spain

SCIENTIFIC POSITIONS AND MEMBERSHIPS

- Academy for Eating Disorders (AED) regular member (Since 2005)
- Student volunteer program assistant-coordinator for the AED (2006-07)
- Member of Oversight Committee of the AED (2008-11)
- External Referee for the European Eating Disorders Review.
- Euroscience Open Forum (ESOF) regular member (Since 2008)

PREDOCTORAL RESEARCH STAGE ABROAD

25/09/07- 02/02/2008: Child and Adolescent Psychiatry, University Hospital Vienna, Austria; **Prof. Andreas Karwautz**

29/05/07- 01/08/07: Eating Disorder Unit - King's College London, Institute of Psychiatry; **Prof. Janet Treasure**

07/2006 - 09/2006: Eating Disorder Unit - University of Chapel Hill, North Carolina, USA; **Prof. Cynthia. M. Bulik**

STUDENTSHIPS/ FELLOWSHIPS

- **AED Student Research Grants Program 2008** to conduct a cross-cultural comparison study of disordered eating behaviour between Cuban and Spanish university students (2008-09).

- **Beca Extranjera (BE) (Foreign Studentship) AGAUR: 2007 BE-100172** for a placement in London, King's College London, Institute of Psychiatry with Prof. Janet Treasure.

- **AED Student/ Early Career Investigator Travel Fellowship** for the International Conference on Eating Disorders, May 2-5, 2007, Baltimore, Maryland.

- **FI (2005 FI 00425):** 4 year studentship for predoctoral studies from the Catalan government.

AWARDS

- **Best Poster Award (Mención de Honor para el Mejor Poster**) for the poster "Associacion entre habitos alimentarios durante la infancia y actitudes parentales respecto a la alimentacion: un estudio europeo multicentrico" (Authors: **Krug, I.,** Bellodi, L., Breceli, J., Collier, D., Karwautz,A., Nacmias, B., Roser, G., Tchanturia, K., Treasure, J., Wagner, G., Fernandez-Aranda, F.) 4º Congreso Hispano Latinomareicano de Trastornos de la Conducta Alimentaria, Barcelona, 6 th of June, 2006.

- **Mención de Honor** for the poster: Un modelo animal de aprendizaje de la conducta de atracon: el papel del condicionamiento y de la densidad energética de la comida (Autores: J. Sansa; I. Krug; VD. Chamizo; F. Fernández-Aranda). 4º Congreso Hispano Latinoamericano sobre Trastornos de la Alimentación, Barcelona, 6 th of June, 2006.

SKILLS & LANGUAGE COURSES

Language Skills: German (native), Spanish (fluent), English (fluent), French (fluent), Turkish (conversational), Italian (conversational), Catalan (completed Level 1)

09-12/2004	**Universidad de Barcelona, Spain**
Summer 2002	**Universitat de Perugia, Italy**
Summer 2000	**Universite de la Sorbonne, Paris, France**
Summer 1998	**L´Ecole International de Cannes, France**
April 1998	**Eurocentre, Paris, France**
Summer 1996/1997	**ELS Language Centre, Chicago, USA**
Summer 1995	**Institute of English Language Studies in Malta**

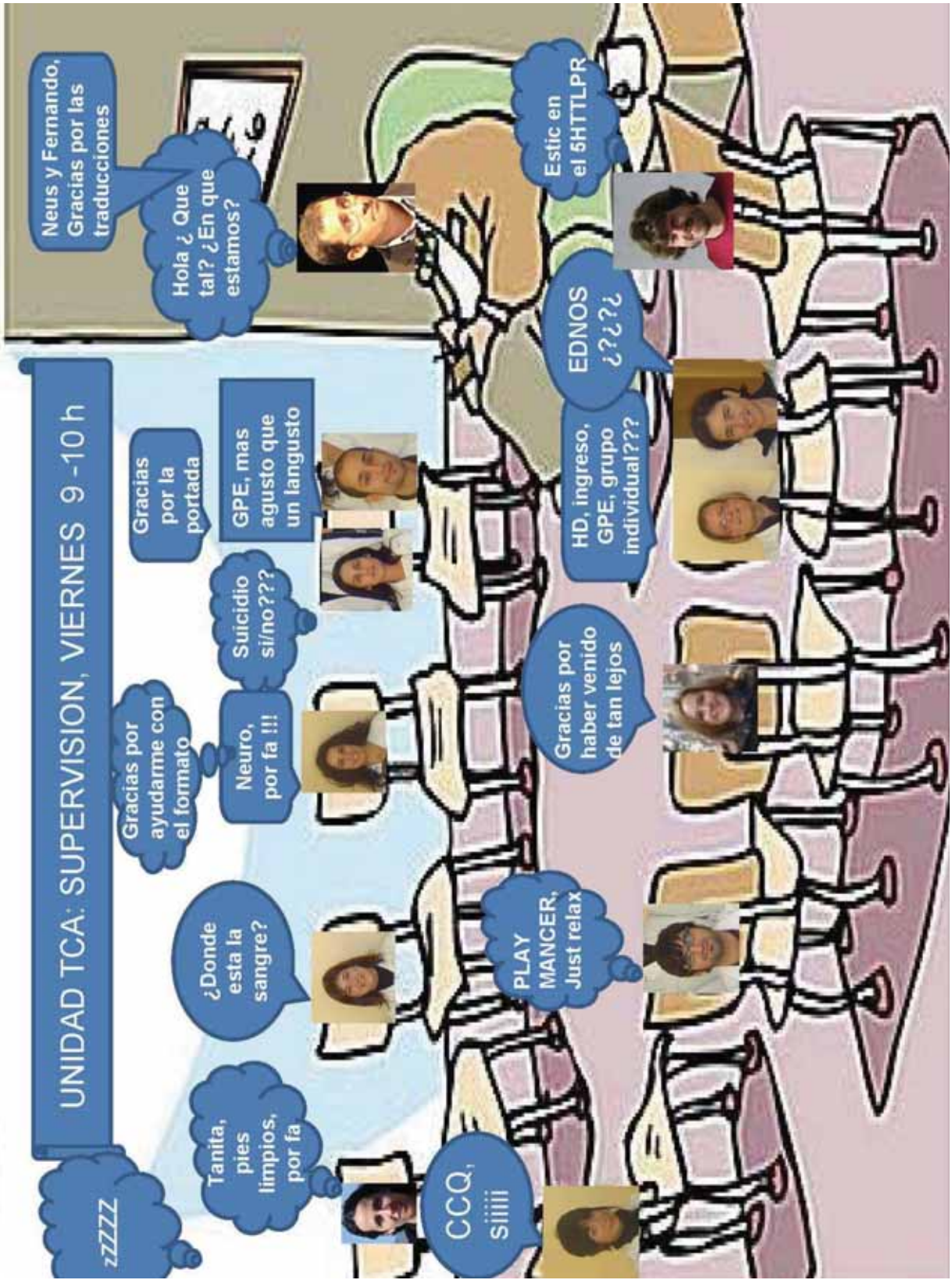
OTHER ACADEMIC OR SCIENTIFICAL MERITS

1.) Volunteering at the Euroscience Open Forum (ESOF, 2008), Science for a better life, Barcelona, July 18-22.

2.) Jornades Doctorials AGAUR (2007). Desenvolupament Professional dels Doctors i Formacio en la Gestio de I'R+I. Generalitat de Catalunya, Departament d'Innovacio, Universitats i Empresas, Collbato, Motnserrat, 19-22 of March.

3.) Formacio Entrevistes Motivacionals de Nivell I (Training in Motivational Interviewing) (2006), Hospital Universitario de Bellvitge, Barcelona, 26-28 of January.

4.) Formación Continuada de Personal Investigador para la Utilización de Animales para la Experimentación y para otros Finalidades Científicos (Training in personal investigator for the use of experiments conducted with animals) (2005). Generalitat de Catalunya, Departament de Medi Ambient i Habitage, Barcelona, 14-18 of March and 4-11 of April.


UNIDAD TCA: SUPERVISION, VIERNES 9 -10 h
zZZZZ
CCQ, siiii
Tanita, pies limpios, por fa
¿Donde esta la sangre?
Gracias por ayudarme con el formato
Neuro, por fa !!!
Suicidio si/no???
Gracias por la portada
GPE, mas agusto que un langusto
PLAY MANCER, Just relax
Gracias por haber venido de tan lejos
HD, ingreso, GPE, grupo individual???
EDNOS ¿?¿?¿
Hola ¿ Que tal? ¿En que estamos?
Neus y Fernando, Gracias por las traducciones
Estic en el 5HTTLPR