RESEARCH ARTICLE

Meta-Analysis on Drugs in People with Eating Disorders

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Abstract

Objective: The aim of this study was to examine whether drug use (DU) is higher in people with eating disorders (EDs) compared to a healthy control group and to perform a meta-analysis on the literature related to DU in people with EDs.
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. A total of 16 papers fulfilled the inclusion criteria and were 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 nervosa (BN, $\delta = 0.462$, $p = < .001$), smaller in binge eating disorder ($\delta = 0.14$, $p < .05$) and non-significant in anorexia nervosa (AN, $\delta = -.167$, $p = .070$).
Conclusions: The differential risk observed in patients with BN might be related to differences in temperament or might be the result of reward sensitization.

Keywords

systematic review; anorexia nervosa; bulimia nervosa; binge eating disorders; drug use

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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. Corcos, Nezelof, Speranza, Topa, Girardon, & Guilbaud, 2001; Krug, Treasure, Anderluh, Bellodi, Cellini, & di Bernardo, 2008; Root, Poyastro Pinheiro, Thornton, Strober, Fernández-Aranda, & Brandt, 2009; Wiederman & Pryor, 1996a,b). 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 anorexia nervosa (AN) and 41% with bulimia nervosa (BN) suffered from co-occurring substance use disorders. However, researchers on this topic have commonly treated substances as one homogenous group (Holderness, Brooks-Gunn, & Warren, 1994; Wiederman & Pryor, 1996a,b). Only more recent investigations looked at a variety of licit and illicit substances separately (e.g. Bulik, Klump,

Thornton, Kaplan, Devlin, & Fichter, 2004; Piran & Gadalla, 2007).

Accordingly, a recent meta-analysis on the comorbidity of alcohol use disorders in EDs has summarized and collated the existing data in the literature (Piran & Gadalla, 2007). As regards to drug use (DU), the synthesis of the literature in EDs has however not yet been adequately updated. With the exception of two theoretical reviews (Pirim & Ikiz, 2004; Wolfe & Maisto, 2000) there is no contemporary empirical review on 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.

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 (Gadalla & Piran, 2007; McCabe & Boyd, 2005; Piran & Gadalla, 2007; Piran & Robinson, 2006a,b; Root et al., 2009; Wiederman & Pryor, 1996a,b). Some 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 (Jordan, Joyce, Carter, Horn, McIntosh, & Luty, 2003; Nagata, Kawarada, Ohshima, Iketani, & Kiriiko, 2002). 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 (Gadalla & Piran, 2007; Nappo, Tabach, Noto, Galduroz, & Carlini, 2002). The 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 & Boyd, 2005; Piran & Robinson, 2006a,b).

Understanding the link between addictions and bulimic symptomatology, especially binge eating, has also been increased by the development of animal models (Boggiano, Artiga, Pritchett, Chandler-Laney, Smith, & Eldridge, 2007; Boggiano & Chandler, 2006). Animals 'binge eat' if they are exposed to some of the environmental factors (food restriction, stress, intermittent exposure to highly palatable food etc.) thought to play a role in the development of human EDs (Avena, Long, & Hoebel, 2005; Corwin, 2006; Corwin & Buda-Levin, 2004; Corwin & Hajnal, 2005; Lewis, Rada, Johnson, Avena, Leibowitz, & Hoebel, 2005; Rada, Avena, & Hoebel, 2005). Furthermore, research has shown 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 (Avena & Hoebel, 2003; Thiele, Stewart, Badia-Elder, Geary, Massi, & Leibowitz, 2004). The theory developed to explain the result of these animal experiments is that palatable food in certain conditions may produce over sensitivity of the reward circuits as happens with DU (Koob & Le Moal, 2005; Robinson & Berridge, 2003). The mechanism underpinning the development of such addictive behaviours is thought to be due to an imbalance in the chemical transmitters of the reward pathways.

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 clinical 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 (Nappo et al., 2002; Piran & Robinson, 2006b).

The aim of this systematic review was therefore to collate, summarize and perform a meta-analysis wherever 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 eating disturbed individuals than in a matched comparison group; specifically, DU would be higher in people with bulimic features. Also, we hypothesized that these individuals would consume more drugs comprising appetite suppressant than stimulating properties.

Methods

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: *EDs, eating problems, unhealthy eating, AN, BN, 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, DU, 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.

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 DU, we considered in this review any frequency of DU, without distinction regarding to its severity) of any sort of illegal DU (or an inappropriate 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.

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).

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 DU because we considered these data more accurate (except in Telch and Stice, 1998, because there is no case with current DU), and last year over last month because we considered last year more representative data of people's DU (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 DU.

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). 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

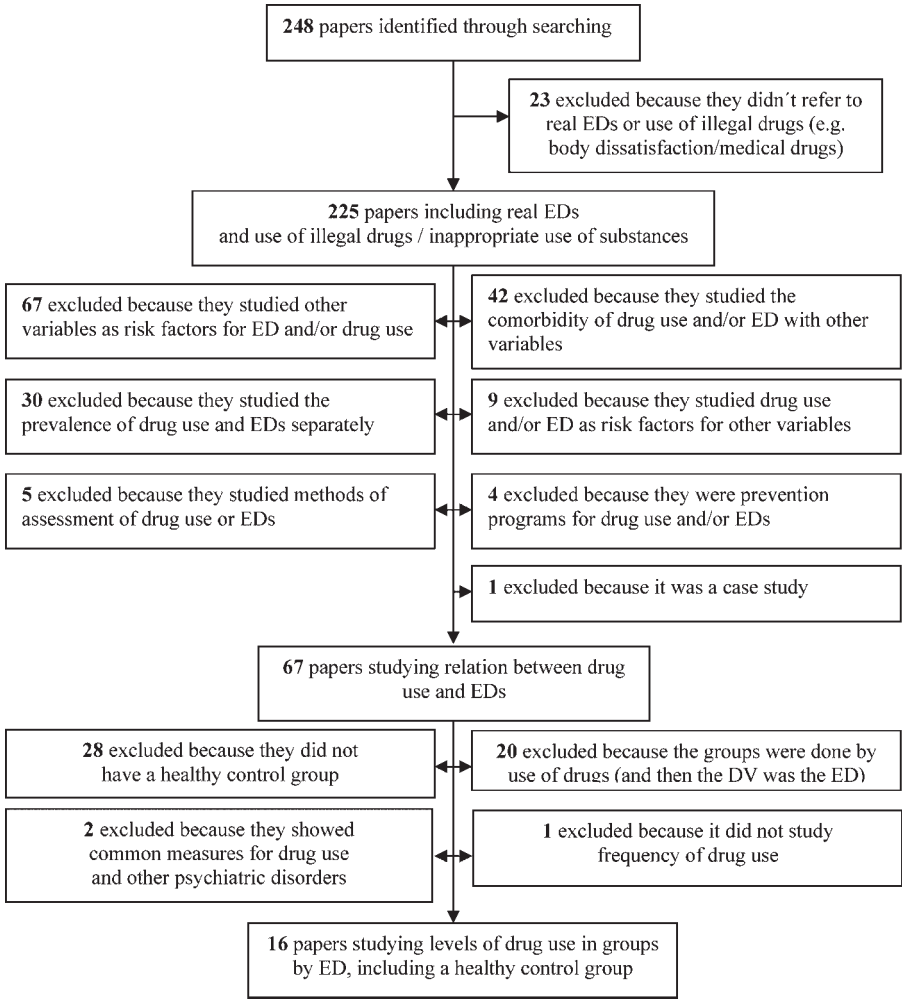

Figure 1 Map of selection procedure

more frequent in the current scientific literature (Lipsey & Wilson, 2001). Cohen's effect sizes are understood as *negligible* (≥ -0.15 and $<.15$), *small* ($\geq .15$ and $<.40$), *medium* ($\geq .40$ and $<.75$), *large* $\geq .75$ and <1.10), *very large* (≥ 1.10 and <1.45) and *huge* (>1.45) (Cohen, 1988). 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 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* (Bradburn & Deeks, 1998) and *metabias* (Steichen, 1998). 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). Random-effect models were used (Everitt, 2003) 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

Table 1 Characteristics of the sample

Study	Sample		Mean age (SD) or age range	Type of sample	Measure of ED	Measure of drugs	% of drug use
	Group	*N*					
Bushnell et al.)	Clinical BN	25 f	M = 23.5 (4.9)	Clinical	Diagnosis interview schedule	Diagnosis interview schedule	Drug abuse. Lifetime: 32%
(1994	Community BN	20 f	M = 27.2 (6.3)	Community	(DIS), version 3A	(DIS), version 3A	Drug abuse. Lifetime: 24%
	HC	777 f	18–44 years	Community			Drug abuse. Lifetime: 6%
Baptista et al.)	BN	22 f	M = 25.3 (6.6)	University	Self-questionnaire	Self-questionnaire (not specified.	Illicit drugs. Lifetime: 13.6%
(1996	BED	97 f	M = 27.8 (8.2)	University	(not specified. Available	Available upon request)	Illicit drugs. Lifetime: 7.7%
	HC	439 f	M = 26.1 (6.5)	University	upon request)		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 and Fairburn (1996)	BN	102 f	M = 23.7 (4.9)	Community	Eating disorder examination (EDE) interview	Semistructured interview designed ad 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 and 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 (TFEO; 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%

(*Continues*)

Table 1 (Continued)

Study	Sample		Mean age (SD) or age range	Type of sample	Measure of ED	Measure of drugs	% of drug use
	Group	*N*					
Ross and Ivis (1999)	Past BED	62 m 111 f	M = 15.2 (2.2)	Community	Questionnaire designed *ad hoc*	Questionnaire designed ad hoc	Last year: Cannabis = 17.7%; Other drugs = 11.1% Last year: Cannabis = 25.0%; Other drugs = 19.8%
	Binge/No purgers	155 m 195 f	M = 15.2 (1.9)	Community			Last year: Cannabis = 39.0%; Other drugs = 23.9% Last year: Cannabis = 33.7%; Other drugs = 19.5%
	Binge/Purgers	46 m 167 f	M = 15.4 (1.8)	Community			Last year: Cannabis = 43.5%; Other drugs = 39.1% Last year: Cannabis = 44.6%; Other drugs = 51.2%
	HC	625 m 558 f	M = 14.8 (2.2)	Community			Last year: Cannabis = 21.6%; Other drugs = 15.1% 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 163 f	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% Lifetime: Marijuana = 44.9%; Heroin = 21.3%; Cocaine = 5.1%
	HC	581 m 500 f		Community			Lifetime: Marijuana = 30.3%; Heroin = 9.7%; Cocaine = 2.0% 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%
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 and 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%

(Continues)

Table 1 (Continued)

Study	Sample		Mean age (SD) or age range	Type of sample	Measure of ED	Measure of drugs	% of drug use
	Group	*N*					
Piran and 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 and 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%

[*] 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 analysed, but not the data from parents.
[§] In these studies we only analyse the data from the first analysis, as the groups were selected based on specific eating disorders behaviours.

(Higgins and Thompson, 2003). I^2 ranges between 0% (no inconsistency) and 100% with values of 25, 50 and 75% were indicative of low, moderate and high heterogeneity, respectively. 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 (Egger & Smith, 1997) and Begg's adjusted rank test (Begg & Mazumdar, 1994), implemented in *metabias*. The last mentioned are significant tests to identify publication bias and, as they have a low power if there are small numbers of studies, we decided to calculate both of them to increase the reliability of the conclusions. Then *fill-and-trim* procedure for the correction of publication bias was used, which calculates which the effect size would be in case there was no publication bias.

Results

Study characteristics

Table 1 summarizes 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 DU differed between studies (clinical interviews, self-questionnaires or surveys, some of them elaborated *ad hoc*). Some studies ($n = 6$) described groups by DSM categories (BN, binge eating disorders or AN) 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 six 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 ED history. For the purpose of this study we categorized 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 DU*. Current or last year use was described in seven studies and lifetime consumption in nine studies.

The meta-analysis of drug use in people with eating disorders

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 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 DU.

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 $\delta = .119$ to $\delta = .428$, that is, in case there was no publication bias, the effect size may be medium.

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

Seven studies (Cance, Ashley, & Penne, 2005; Gutiérrez, Mora, Unikel, Villatoro, & Medina-Mora, 2001; Lock, Reisel, & Steiner, 2001; Piran & Robinson, 2006a,b; Stock, Goldberg, Corbett, & Katzman, 2002; Welch & Fairburn, 1996;) described *stimulant DU, with a total of 25 independent comparisons*. The meta-analysis showed

an effect size which was not statistically significant ($\delta = -.084$, $z = 0.73$, $p = .46$). There was evidence of heterogeneity between studies ($X^2_{(24)} = 492.32$, $p < .001$) and also a high index of inconsistency across the studies ($I^2 = 95.1\%$). In contrast to the visual inspection of funnel plot[1], 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 $\delta = .357$ (estimated small effect size in case there was no publication bias).

Twelve studies described *use of opiates-cannabis* (Cance et al., 2005; Devaud, Jeannin, Narring, Ferron, & Michaud, 1998; Dunn, Larimer, & Neighbors, 2002; Gutiérrez et al., 2001; Lock et al., 2001; Neumark-Sztainer, Story, & French, 1996; Piran & Gadalla, 2007; Piran & Robinson, 2006a,b; Ross & Ivis, 1999; Stock et al., 2002; Welch & Fairburn, 1996) with a total of 24 comparisons in different EDs. 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 $\delta = .458$ achieved with fill-and-trim method. Due to the extended use of cannabis in the general population, we tried to analyse 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 ($z = 3.13$, $p = .002$).

Seven studies described other drugs (Cance et al., 2005; Dunn et al., 2002; Gutiérrez et al., 2001; Piran & Robinson, 2006a,b; Stock et al., 2002; Welch & Fairburn, 1996) with a total of 17 comparisons, with non-significant pooled standardized effect sizes in the whole group ($\delta = .047$, $z = 0.39$, $p = .69$) and also considering the subgroup *hallucinogens* separately ($\delta = -.020$, $z = 0.15$, $p = .88$). We analysed 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 $\delta = .411$ (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 of any kind of drugs (Baptista, Sampaio, do Carmo, Reis, & Galvao-Teles, 1996; Bushnell, Wells, McKenzie, Hornblow, Oakley-Browne, & Joyce, 1994; Halvorsen, Andersen, & Heyerdahl, 2005; Ross & Ivis, 1999; Telch & Stice, 1998) and a total number of nine independent comparisons. In this case we found a medium and significant pooled standardized effect size ($\delta = .509$, $z = 3.73$, $p < .001$). 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 was performed.

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

Four studies analysed DU in the group *AN-restrictors* (Halvorsen et al., 2005; Piran & Robinson, 2006a,b; Stock et al., 2002) with a total number of 20 independent comparisons. The meta-analysis showed a non-significant standardized effect size ($\delta = -.167$, $z = 1.81$, $p = .07$) (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.

In the group of *BN-purgers* there are eight studies (Baptista et al., 1996; Bushnell et al., 1994; Cance et al., 2005; Devaud et al., 1998; Dunn et al., 2002; Piran &

[1] The forrest plots are not included in this section due to lack of space. A copy of them is available upon request.

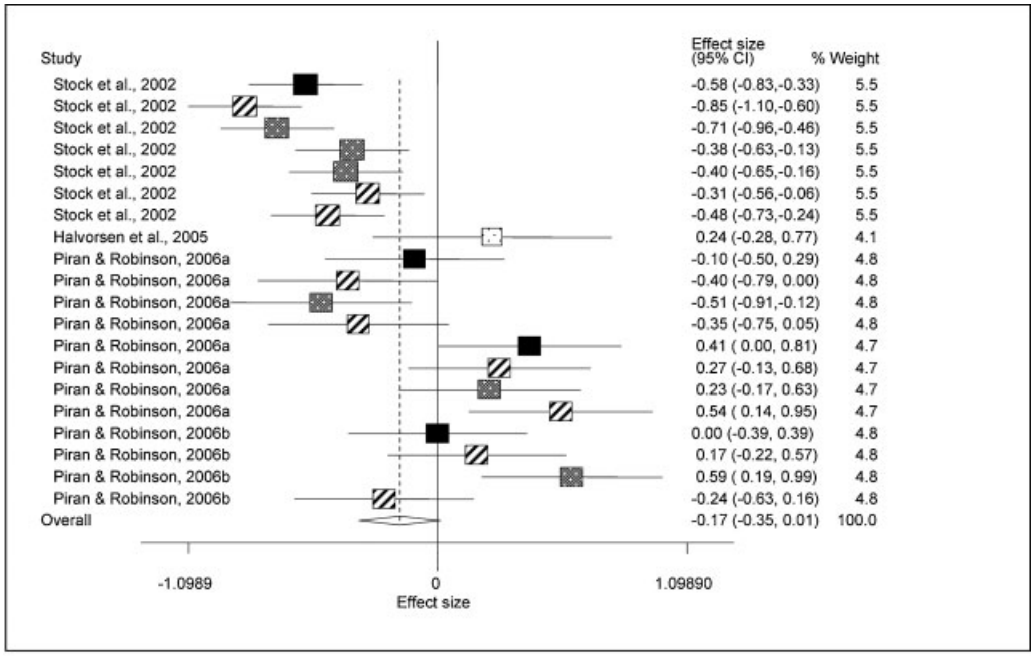

Figure 2 Forrest plot of meta-analysis for the AN-restrictors group

Robinson, 2006a; Ross & Ivis, 1999; Welch & Fairburn, 1996) 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 $\delta = .462$ to $\delta = .530$.

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* (Baptista et al., 1996; Dunn et al. 2002; Piran & Robinson, 2006a,b; Ross & Ivis, 1999; Telch & Stice, 1998), 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 $\delta = .141$ to $\delta = .252$. There were no differences in the effect sizes in relation to the drugs used.

Finally, there were four studies using *general ED/high risk of ED* categories (Gutiérrez et al., 2001; Lock et al., 2001; Neumark-Sztainer et al., 1996; Piran & Gadalla, 2007), with a total of 13 independent comparisons. In this group of studies the meta-analysis revealed a pooled standardized effect size of nearly 0 ($\delta = -.045$, $z = 0.37$; $p = .07$). 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 $\delta = .407$ (medium estimated effect size in case there was no publication bias).

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 standardized effect sizes. The meta-analysis was carried out initially clustering all types of ED together,

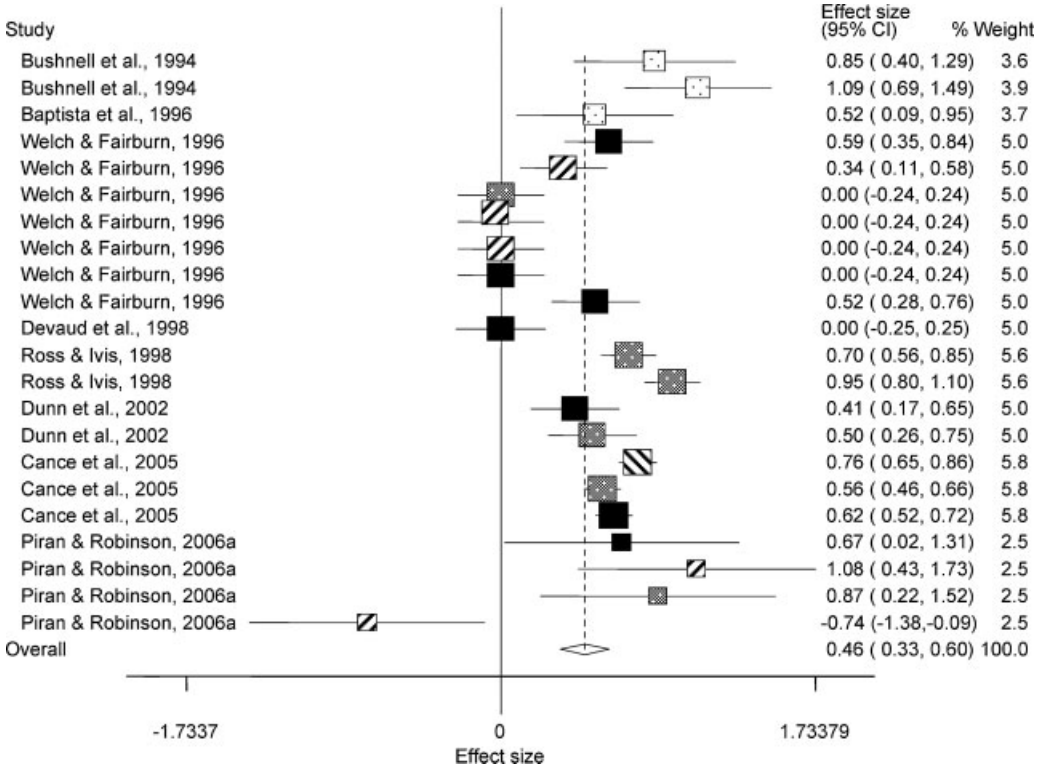

Figure 3 Forrest plot of meta-analysis for the BN-purgers group

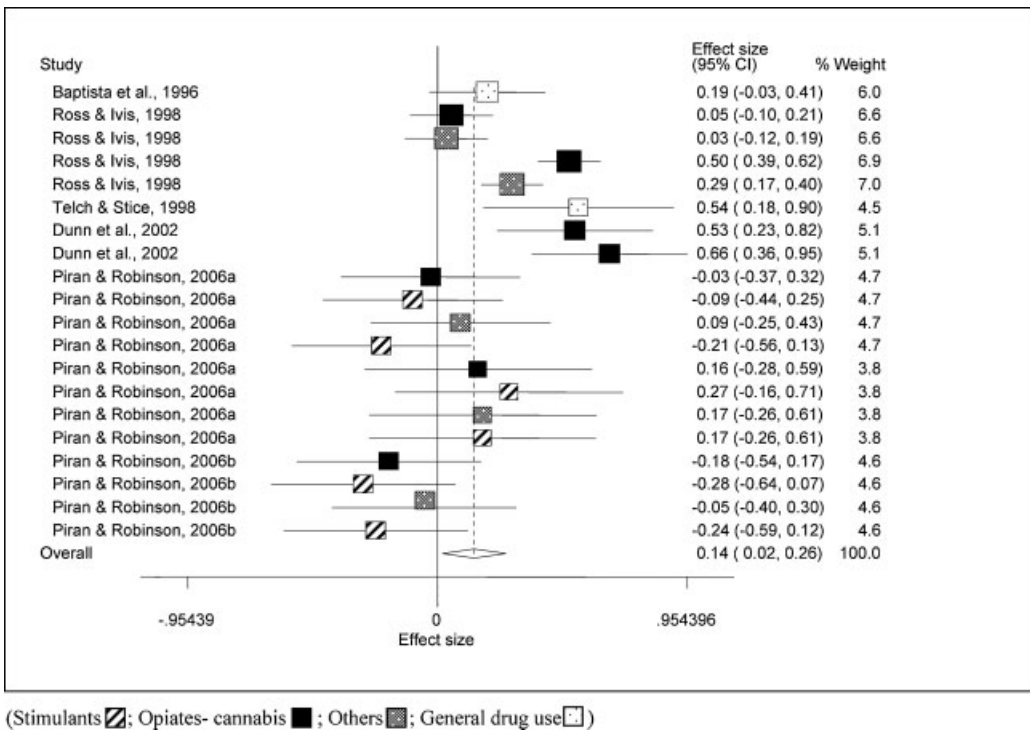

Figure 4 Forrest plot of meta-analysis for the BED-bingers group

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 DU was found particularly for *bulimia/purgers*, the prevalence was lower for *binge eating disorder/bingers* and people from the group *anorexia/restrictors* had lower levels of DU than the healthy population.

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 (Holderness et al., 1994; Krug et al., 2008; Pirim & Ikiz, 2004; Wolfe & Maisto, 2000). However the effect size in the present review was only negligible. This result could in part be due to the heterogeneity resulting from combining ED subtypes and DU categories because, and as it will be explained later, there are important differences in the results between restrictive AN and binge/purging ED individuals regarding general DU and the use of specific drug types. Partially, this result could also 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 Berkońs bias (Berkson, 1946).

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 (Herzog, Franko, Dorer, Keel, Jackson, & Manzo, 2006; Nappo et al., 2002; Root et al., 2009) 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 (Nappo et al., 2002). The results regarding the different types of DU may be explained according to the case mix in each of the analyses: in the two analyses with significant effect sizes (*opiates-cannabis* and *general drug use*) a large proportion of BN-purgers or BED-bingers patients were incorporated, whereas in the other two analyses, without significant effect sizes (*stimulants* and *others*), individuals with different ED diagnoses, including AN-restrictors, were present. However, it should be noted that the number of studies was small for each of the assessed drug categories, rendering statistical power low.

Drug use in specific subgroups of eating disorders

The results confirmed our third hypothesis, which was that DU would be higher in people with BN. A moderate sized increase in DU of all categories was found in this ED subtype. People from the group *binge eating disorder/bingers* also revealed a small and significant increased risk of DU. In contrast, people from the group *anorexia/restrictors* do not seem to have an increased probability for DU, as the meta-analysis showed a non-significant 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 (Gadalla & Piran, 2007; Holderness et al., 1994; Krug, Bulik, Strober, Jiménez-Murcia, Granero, & Agüera, 2009; Root et al., 2009). The number of studies which split the *anorexia/restrictors* group into the bulimic and restrictive subcategories was too small to undertake separate meaningful comparisons. In relation to the sub group *general ED/high risk of ED* we were not able to reveal a significant effect size. This finding could in part be attributable to the fact that these studies may have included a considerable amount of restrictors in the samples. It should also be acknowledged that the definition of 'risk of ED' in these studies are very different and usually include a wide range of symptoms, which could also imply different tendencies to DU.

The increased risk of substance use in people with bulimic symptomatology (including *binge eating disorder/bingers*) might also be related to differences in temperament such as an increased novelty seeking. This finding is also in line with other studies (Álvarez-Moya et al., 2007; Fernández-Aranda, Jiménez-Murcia, Álvarez-Moya, Granero, Vallejo, & Bulik, 2006; Krug et al., 2009; Leyton, 2007). Novelty seeking has been associated with specific neurochemical correlates, i.e. norepinephrine deregulation (Ham, Choi, Lee, Kang, & Lee, 2005; Weinshenker & Schroeder, 2007) and dopaminergic disturbances (Keltikangas-Järvinen, Räikkönen, Ekelund, & Peltonen, 2004). Impulsivity could be another candidate feature shared by the individuals who present with an ED and DU (Álvarez-Moya et al., 2007; Fernández-Aranda et al., 2006; Fernández-Aranda, Poyastro Pinheiro, Thornton, Berrettini, Crow, & Fichter, 2008). Although many studies of EDs have explored the extent to which impulsivity is associated with the presence of comorbid DU, 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 DU and other impulsive behaviours (Fichter, Quadflieg, & Rief, 1994; Lacey, 1993; Lacey & Evans, 1986; Nagata, Kawarada, Kiriike, & Iketani, 2000). 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 (Harrison, ÓBrien, López, & Treasure, 2009; Treasure, 2007).

Limitations

The results from the present review should be considered within the context of several limitations. Firstly, there are fewer studies than expected 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 behaviour 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 DU 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.

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 focussed 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 the group *bulimia/purgers*. No association was found between DU and anorexic features. 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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