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REVIEW

Clinical features in co-occuring obsessive-compulsive disorder and bipolar disorder: A systematic review and meta-analysis

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ABSTRACT

Obsessive-compulsive disorder (OCD) frequently co-occurs with various psychiatric conditions and may impact as many as one-fifth of individuals diagnosed with bipolar disorder (BD). Despite the expanding body of literature on the coexistence of OCD and BD, there is a notable lack of comprehensive data pertaining to the distinct features of obsessive-compulsive symptoms that define this comorbidity. To bridge this knowledge gap, we conducted a systematic search of PubMed/MEDLINE, Scopus, EMBASE, and PsycINFO until August 7th, 2023. We performed random-effects meta-analyses to compare individuals with both OCD and BD to those with OCD in terms of OCD symptomatology as well as the specific categories of obsessions and compulsions. Out of the 10,393 records initially screened, 17 studies were ultimately incorporated into the qualitative assessment, with 15 of them being included in the quantitative analysis. Individuals with OCD and BD experienced fewer lifetime contamination obsessions (OR=0.71; 95 %CI=0.53, 0.95; $p = 0.021$) and more sexual obsessions (OR=1.77; 95 %CI=1.03, 3.04; $p = 0.04$) compared to individuals with OCD without BD. No significant difference was observed for other types of obsessions or compulsions or for the severity of OCD symptoms, although BD type may play a role according to meta-regression analyses. The detection of the presence of sexual or contamination obsessions through a detailed interview may be the focus of clinical attention when assessing OCD in the context of comorbid BD. Sub-phenotyping complex clinical presentation of comorbid psychiatric disorders can aid in making more informed decisions when choosing an appropriate treatment approach.

1. Introduction

Comorbidity in psychiatric disorders is the rule rather than the exception. The same holds true for obsessive-compulsive disorder (OCD), a mental health condition characterized by the presence of obsessions and/or compulsions (Grant, 2014). OCD often co-occurs with many other psychiatric disorders (Osland et al., 2018), such as psychotic disorders (Cederlof et al., 2015), anxiety disorders (Murphy et al.,

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2013), major depressive disorder (MDD) (Murphy et al., 2013), substance use disorder (Blom et al., 2011), or bipolar disorder (BD) (Amerio et al., 2014; Cederlof et al., 2015).

BD is a chronic mental illness with a complex etiology (Fico et al., 2022; Lima et al., 2022; Vieta et al., 2018) characterized by recurrent acute affective episodes (i.e., depressive, hipomanic, manic) and periods of absent or sub-threshold symptoms. Nearly one-fifth of people with OCD have a lifetime diagnosis of BD, and a similar prevalence of OCD has been described in people with a primary diagnosis of BD (Amerio et al., 2015). The reasons for the frequent co-occurrence of these two disorders may be explained by the existing commonalities in several genes and molecular pathways, especially involving the dopaminergic systems (Hamidian et al., 2020).

In recent years, the coexistence of OCD-BD has garnered growing attention due to the complexities involved in distinguishing between these disorders and the significant impact on treatment decisions. While selective serotonin reuptake inhibitors (SSRIs) are considered the gold standard for treating OCD (Stein et al., 2019), their use in individuals with BD, particularly at higher doses, may heighten the risk of inducing new manic or mixed episodes (Pacchiarotti et al., 2013). Consequently, there is a pressing need to optimize medication strategies in such cases (Amerio et al., 2019).

When considering the clinical features of OCD in patients with and without a diagnosis of BD, the literature appears to be heterogeneous. In fact, looking at the severity of OCD symptomatology, individual studies report conflicting results, with some revealing more severe symptomatology in both comorbid (Dell'Osso et al., 2020) and non-comorbid groups (Ozdemiroglu et al., 2015), while others showing no significant differences (Shabani and Alizadeh, 2008). The same heterogeneity is observed for specific types of obsessions and compulsions, with certain symptoms (e.g., aggressive or sexual obsessions, checking or ordering compulsions) being more prevalent in one group or the other (Shabani and Alizadeh, 2008; Tukel et al., 2006; Zutshi et al., 2007).

Previous systematic reviews and meta-analyses focusing on OCD-BD comorbidity have mainly investigated the prevalence of both disorders in these populations (Amerio et al., 2015), providing a description of the main predictors of this comorbidity, but lacking a detailed description of the clinical features involved. To date, no systematic review or meta-analysis has been conducted focusing on the clinical differences between OCD-BD and OCD in terms of obsessive-compulsive symptomatology. To fill this gap, we aimed to examine the differences in the obsessive-compulsive symptomatology in people diagnosed with BD and OCD, compared with people diagnosed with OCD without BD, focusing particularly on the types of obsessions and compulsions, the number of obsessions and compulsions, and the severity of obsessive-compulsive symptoms. This could provide a framework for the assessment of patients with OCD comorbid with BD, to enhance the management of individuals with this comorbidity.

2. Material and methods

The present systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021), and its protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) (https://www.crd.york.ac.uk/PROSPERO/; protocol CRD42023392296). Any deviation from the protocol is reported in the Supplementary Materials, Appendix I.

2.1. Search strategy

We systematically searched the PubMed/MEDLINE, Scopus, EMBASE, and PsycINFO databases from inception to August 7th, 2023. The search strategies are detailed in the Supplementary Materials, Appendix II. To identify potential additional studies not captured by the original search string, the references of each included study, textbooks, and other materials were hand searched.

2.2. Eligibility criteria and study outcomes

Original studies providing quantitative data about the clinical characteristics of OCD (i.e., type or number of obsessions, type or number of compulsions, symptom severity scale scores) in people diagnosed with OCD with and without BD comorbidity were eligible for inclusion. Psychiatric diagnoses were required to be made according to the Diagnostic and Statistical Manual for Mental Disorders (DSM) (APA, 1994, 2000, 2013) or the International Classification of Diseases (ICD) (WHO, 2004) diagnostic criteria. No language, age, or sample size restrictions were applied. We considered for inclusion both observational and interventional studies: for longitudinal observational studies, baseline data were preferred, but if not available, data from the first follow-up were collected; for interventional studies, only baseline data were considered. In cases where the populations of multiple studies overlapped, we included the largest study with the most representative data relevant to our aims. Reviews (no original data), case reports and case series (no reliable control group), and studies conducted on animals (population not covered by our criteria) were excluded.

2.3. Study selection and data extraction

Four groups of two authors each (MDP and CT, RS and CTL, VO and LB, NG and MM) independently reviewed studies of potential interest, and a third author (CP, EV, or GF) was consulted when a consensus could not be reached. Data extraction included (when available): first author, publication year, geographical region and country, study design, diagnostic criteria and (semi)structured interview adopted, setting of the study, age group (i.e., children/adolescents, adults, older adults, or mixed) of included sample, number of people with OCD and people with OCD and BD, type of outcome (e.g., type of obsessions, type of compulsions, symptoms severity scale scores), mean and standard deviation (SD) of the outcome or number of events for both groups, mean age, years of education, age at onset of OCD, duration of illness, % of females, % of people with comorbid physical conditions, mean score at symptom severity scales, number of episodes,% of people with comorbid psychiatric disorders, % of patients under psychotropic medication, OCD course, and % of people with history of suicide attempts for both people with OCD and people with OCD and BD, age at onset of BD, % of people diagnosed with BD-I, and% of euthymic, depressed, or (hypo)manic patients only for people with BD and OCD. We used WebPlotDigitizer to extract numerical variables from graphs when required (https://automeris.io/WebPlotDigitizer/). When information was not available, we contacted the authors to request the relevant data.

2.4. Methodological quality appraisal

Three authors (LB, NG, and MM) independently assessed the risk of bias in the included studies, and a third author (MDP or CP) resolved any disagreements. The Newcastle-Ottawa Scale (NOS) (Stang, 2010) was used to rate the quality of observational studies, and NOS scores were converted to "Agency for Healthcare Research and Quality" (AHRQ) standards, as done elsewhere (Fornaro et al., 2022).

2.5. Statistical analyses

We conducted the meta-analyses using a random-effect model (restricted maximum-likelihood estimator) (Harville, 1977) with the R-package "metafor" (Viechtbauer and Viechtbauer, 2015), using RStudio R version 4.1.2 (R Core Team, 2021). For continuous outcomes (i.e., symptoms severity scale scores, number of obsessions, number of compulsions), we used the standardized mean difference (SMD), represented by Hedge's g, as the effect size; for dichotomous outcomes (i.e., frequency of specific types of obsessions and compulsions), we used the

odds ratio (OR) as the effect size. Leave-one-out sensitivity analyses were conducted by (i) excluding one study at a time from the main analysis, and by (ii) including only good-quality studies according to AHRQ standards. We assessed heterogeneity by using Cochran's Q test (Cochran, 1950), τ^2 and I^2 statistics (Higgins et al., 2019), and we adopted the graphical display of study heterogeneity (GOSH) method (Olkin et al., 2012) to graphically explore it when at least five studies were available. Whenever Cochran's Q test presented a $p < 0.10$, or the I^2 statistic showed a value >50 %, subgroup and meta-regression analyses were conducted according to dichotomic (i.e., primary or secondary outcome) and continuous predictors (i.e., mean age, age at onset of BD or OCD, duration of illness of BD or OCD, % of females, % of BD-I, % of euthymic, % of depressed, % of (hypo)manic, % of people with OCD and lifetime comorbid MDD, symptoms severity scale). Prediction intervals were calculated. Publication bias was explored by visually examining funnel plots and using Egger's test (Egger et al., 1997) when at least ten studies were included in the analysis.

3. Results

A total of 10,393 references were identified from various sources. After duplicate removal, 6568 studies were further screened. Among these, 6339 were excluded at the title/abstract level, 210 after the full-text evaluation, and two were not retrieved. Finally, 17 studies were included in the present systematic review, of which 15 (Centorrino et al., 2006b; de Filippis et al., 2018b; Dell'Osso et al., 2020; Domingues-Castro et al., 2019a; Fistikci et al., 2012; Joshi et al., 2010; Khalkhali et al., 2022; Mahasuar et al., 2011b; Ozdemiroglu et al., 2015; Perugi et al., 1997; Rigardetto et al., 2011; Shabani and Alizadeh, 2008; Timpano et al., 2012; Tukel et al., 2006; Zutshi et al., 2007) provided sufficient data to perform a meta-analysis. The PRISMA flowchart is reported in Fig. 1. The studies excluded from this review are detailed in the Supplementary Materials, Appendix III.

3.1. Characteristics of included studies

The 17 studies included were published between 1997 and 2022. The total number of people with OCD-BD was 682 (range=16–88) compared to 3162 (range=17–881) people with OCD. Fourteen studies were cross-sectional, and three were prospective-cohort studies. Thirteen studies focused on adult patients, three included children/adolescents, and one considered both adults and children/adolescents in its sample.

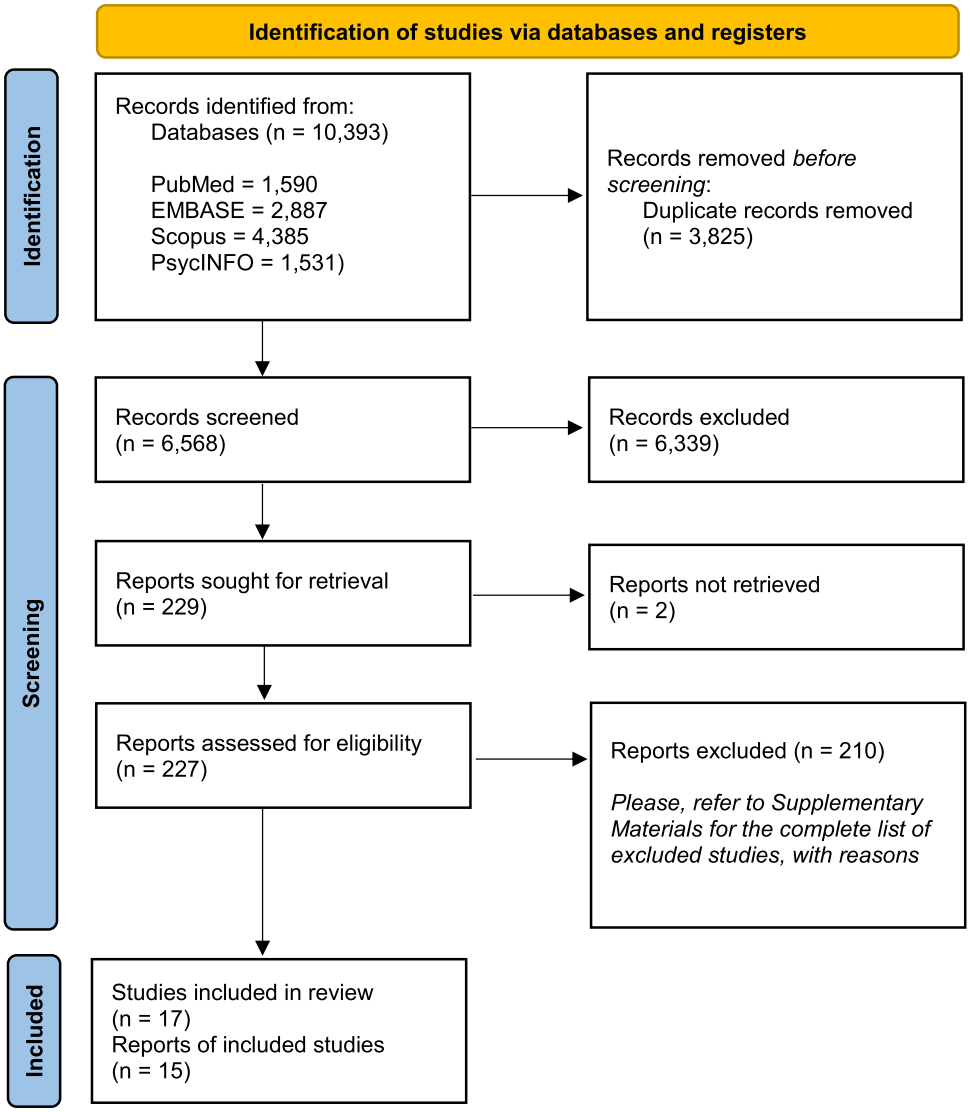

Fig. 1. PRISMA flowchart, 2020 edition, adapted. *From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/.

The mean age of people diagnosed with OCD-BD was 30.84 (±9.05) years, with an age at onset of OCD of 16.19 (±6.81) years, an age at onset of BD of 14.37 (±4.52) years, and a duration of illness of 14.18 (±8.67) years; 46.6 % of the participants were female. Five studies reported the prevalence of episodic OCD (48.3 %, range=34–75). Fourteen studies reported information about the type of BD; among these, 38.5 % (range=2–82) of the included patients were diagnosed with BD type I. Regarding mood state, nine studies provided data: 88.9 % of the sample were euthymic, 7.4 % were depressed, 3.5 % were (hypo)manic, and 0.2 % experienced a mixed episode.

The mean age of people diagnosed with OCD was 33.31 (±9.11) years, with an age at onset of 16.37 (±8.24) years, and a duration of illness of 10.51 (±7.39) years; 53.5 % of the participants were female. Although these patients did not have comorbidity with BD, lifetime comorbidity with MDD was explored in 11 studies (47 %, range=30–71). Six studies reported the prevalence of episodic OCD (18.6 %, range=3–27).

Additional information on the studies included in the systematic review and meta-analysis is presented in Table 1 and Supplementary Materials, Appendix IV.

3.2. Main analyses

The main results of the meta-analyses conducted are displayed in Table 2 and Fig. 2.

People with OCD comorbid with BD showed significantly fewer contamination obsessions (OR=0.71; 95 %CI=0.53, 0.95; p-value=0.021), and more sexual obsessions (OR=1.77; 95 %CI=1.03, 3.04; p-value=0.04), than those diagnosed with OCD without BD. No significant differences were found in the frequency of other types of obsessions or compulsions or in the OCD symptom severity scales.

Additional details on the main analyses are presented in the Supplementary Materials, Appendix V.

3.3. Meta-regression analyses

We conducted meta-regression analyses to explore the role of dichotomous and continuous predictors on obsessive-compulsive symptomatology and on the frequency of specific obsessions and compulsions. In particular:

(i) decreasing% of people with BD-I in the sample (β= −1.99) significantly predicted higher OCD total symptom scores in the OCD-BD group; (ii) decreasing% of people with BD-I in the sample (β= −2.5) significantly predicted higher obsessive symptom scores in the OCD-BD group; (iii) lower age at onset of OCD among people with OCD-BD (β= −0.06) significantly predicted higher compulsive symptom scores in the OCD-BD group; (iv) increasing% of females among people with OCD-BD (β=2.42) significantly predicted higher number of obsessions in the OCD-BD group; (v) higher age among people with OCD-BD (β=0.11) significantly predicted higher frequency of symmetry/exactness obsessions in the OCD-BD group; (vi) higher age at onset of OCD among people with OCD-BD (β=0.53) significantly predicted higher frequency of pathological doubts in the OCD-BD group; (vii) decreasing% of people with BD-I in the sample (β= −1.53) and increasing% of people with lifetime MDD comorbidity among people with OCD (β=3.52) significantly predicted higher number of compulsions in the OCD-BD group; (viii) increasing% of females among people with OCD-BD (β= −1.97) significantly predicted lower frequency of cleaning/washing compulsions in the OCD-BD group; ix) increasing% of people in (hypo)mania (β=4.3) significantly predicted higher frequency of hoarding/collecting compulsions in the OCD-BD group.

Additional details on the meta-regression analyses are presented in the Supplementary Materials, Appendix V.

3.4. Sensitivity analyses

Leave-one-out sensitivity analyses were performed. In particular:

(i) By removing (Dell'Osso et al., 2020) from the comparison relative to total OCD symptomatology, the difference became significant and similar in magnitude; (ii) by removing (Shabani and Alizadeh, 2008) or (Zutshi et al., 2007) from the comparison relative to contamination obsessions, the difference became not significant and similar in magnitude; (iii) by removing any study from the comparison relative to sexual obsessions, with the exception of (Tukel et al., 2006; Zutshi et al., 2007), the difference became not significant and similar in magnitude; (iv) by removing (Zutshi et al., 2007) from the comparison relative to hoarding/saving obsessions, the difference became significant and similar in magnitude; (v) by removing (Mahasuar et al., 2011b) from the comparison relative to the number of compulsions, the difference became significant and passed from a very small to a small effect size; (vi) by removing (Joshi et al., 2010) or (Rigardetto et al., 2011) from the comparison relative to cleaning/washing compulsions, the difference became significant and similar in magnitude; (vii) by removing (Zutshi et al., 2007) from the comparison relative to repeating rituals, the difference became significant and passed from a very small to a small effect size; (viii) by removing (Zutshi et al., 2007) from the comparison relative to miscellaneous compulsions, the difference became significant and similar in magnitude.

Additionally, sensitivity analyses by considering good-quality studies only were performed. In particular:

(i) considering the comparison relative to sexual obsessions, the differences between groups became not significant after removing poor- and fair-quality studies;
(ii) considering the comparison relative to cleaning/washing compulsions, the differences between groups became significant after removing poor- and fair-quality studies.

Additional details on the sensitivity analyses and the GOSH plots are presented in the Supplementary Materials, Appendices V–VI.

3.5. Publication bias

When examining the differences in total OCD symptomatology, the Egger test was significant (z= −2.5854; p-value=0.009), indicating the presence of publication bias. No publication bias was detected for the comparisons relative to aggressive obsessions, and cleaning/washing compulsions.

Additional details on the publication bias are presented in the Supplementary Materials, Appendix V.

3.6. Characteristics of the studies and comparisons included in the qualitative synthesis

Two studies (Coskun and Mukaddes, 2008; Masi et al., 2018) could only have been meta-analyzed together due to their unique method of data aggregation, but were only considered in the systematic review to avoid potentially including information from the same subjects multiple times, as it was not clear whether the recruited samples partially overlapped. Both studies were conducted on children/adolescents. The first one (Coskun and Mukaddes, 2008) found that people in the OCD-BD group were more likely to have hoarding obsessions or compulsions compared to people with OCD, with no significant differences regarding aggressive, sexual, religious, somatic, symmetry, and contamination obsessions, or checking, ordering, counting, repeating, cleaning, or washing compulsions. The second study (Masi et al., 2018) confirmed these results using a larger sample size.

Table 1
Characteristics of the studies included in the systematic review and meta-analysis.

Author, year, country	Study design	Setting	Population (n)	Mood state patients with OCD-BD (%)	Mean age	Percentage of females	Diagnostic criteria	Instrument adopted	OCD symptomatology type	Outcome type	Quality of the study (NOS)
Centorrino et al. (2006a), USA	Prospective-cohort	Inpatients	OCD (17) OCD-BD (16)	NA	35.9 ± 10.7 33.7 ± 10.3	66 % 37 %	DSM-IV	OCSS	Total OCD symptomatology	Score	5 (POOR)
de Filippis et al. (2018a), Italy	Cross-sectional	Outpatients	OCD (20) OCD-BD (26)	Euthymic (100)	47.38 ±13.2 42.5 ± 15.5	50 % 69 %	DSM-5 (MINI)	Y-BOCS	Total OCD symptomatology	Score	7 (GOOD)
Dell'Osso et al. (2020), multicenter	Cross-sectional	Outpatients	OCD (369) OCD-BD (32)	Euthymic (76.2) Depressed (23.8)	38.2 ± 13.1 43.7 ± 14.3	60.6 % 56.3 %	DSM-IV (SCID)	Y-BOCS DY-BOCS	Total OCD symptomatology; obsessive symptoms; obsessions distress; compulsive symptoms; compulsions distress	Score	7 (GOOD)
Domingues-Castro et al. (2019b), Brasil	Cross-sectional	NA	OCD (881) OCD-BD (74)	NA	35.9 ± 12.6 34.9 ± 10.7	58 % 57 %	DSM-IV (SCID)	Y-BOCS	Total OCD symptomatology; obsessive symptoms; compulsive symptoms	Score; specific obsessions	6 (GOOD)
Fistikci et al. (2012), Turkey	Cross-sectional	Outpatients	OCD (27) OCD-BD (17)	NA	36.78 ±10.89 34.12 ±10.44	NA NA	DSM-IV (SCID)	Y-BOCS	Obsessive symptoms; compulsive symptoms	Specific obsessions; Specific compulsions	5 (FAIR)
Joshi et al. (2010), USA	Cross-sectional	NA	OCD (106) OCD-BD (19)	Euthymic (56) Manic (47.4)	11.4 ± 3.2 12.5 ± 3	41 % 26 %	DSM-III (K-SADS)	CY-BOCS	Obsessive symptoms; compulsive symptoms	Specific obsessions; Specific compulsions	4 (POOR)
Khalkhali et al. (2022), Iran	Cross-sectional	Outpatients	OCD (94) OCD-BD (44)	Euthymic (100)	39.18 ±12.95 43.95 ±13.31	31 % 30 %	DSM-5	Y-BOCS	Total OCD symptomatology; obsessive symptoms; compulsive symptoms	Score; specific obsessions and compulsions	6 (POOR)
Mahasuar et al. (2011a), India	Cross-sectional	NA	OCD (57) OCD-BD (34)	Euthymic (100)	29.36 ±8.31 28.39 ±7.1	25 % 32 %	DSM-IV (SCID)	Y-BOCS	Total OCD symptomatology; insight; obsessive symptoms; compulsive symptoms	Score; mean number; specific obsessions	8 (GOOD)
Masi et al. (2018), Italy	Prospective-cohort	NA	OCD (169) OCD-BD (88)	NA	13.32 ±2.7 14.2 ± 2.6	30 % 36 %	DSM-IV; DSM-5 (K-SADS)	Y-BOCS	Obsessive symptoms; compulsive symptoms	Specific obsessions and compulsions	6 (GOOD)
Masi et al. (2007), Italy	Prospective-cohort	Mixed	OCD (77) OCD-BD (43)	NA	13.68 ±2.91 13.73 ±2.8	27 % 35 %	DSM-IV (K-SADS)	Y-BOCS	Obsessive symptoms; compulsive symptoms	Specific obsessions and compulsions	6 (GOOD)

(*continued on next page*)

Table 1 (*continued*)

Author, year, country	Study design	Setting	Population (n)	Mood state patients with OCD-BD (%)	Mean age	Percentage of females	Diagnostic criteria	Instrument adopted	OCD symptomatology type	Outcome type	Quality of the study (NOS)
Ozdemiroglu et al. (2015), Turkey	Cross-sectional	Outpatients	OCD (61) OCD-BD (32)	NA	37.7 ± 12.9 36.2 ± 12	62.3% 50%	DSM-IV (SCID)	Y-BOCS	Total OCD symptomatology; obsessive symptoms; compulsive symptoms	Score; mean number; specific obsessions and compulsions	7 (GOOD)
Perugi et al. (1997), Italy	Cross-sectional	Outpatients	OCD (291) OCD-BD (54)	NA	32.5 ± 12.6 32.8 ± 12.2	57.4% 46.3%	DSM-III-R	Specially constructed OCD-questionnaire	Obsessive symptoms; compulsive symptoms	Specific obsessions and compulsions	7 (GOOD)
Rigardetto et al. (2011), Italy	Cross-sectional	Outpatients	OCD (259) OCD-BD (31)	NA	34.2 ± 12 32.8 ± 13.2	49.4 % 16.1 %	DSM-IV (SCID)	Y-BOCS	Total OCD symptomatology; obsessive symptoms; compulsive symptoms	Score; specific obsessions and compulsions	6 (GOOD)
Shabani and Alizadeh (2008), Iran	Cross-sectional	Outpatients and Inpatients	OCD (39) OCD-BD (39)	Euthymic (100 %)	30.1 ± 6.52 26.6 ± 7.23	84.6% 76.9%	DSM-IV (SCID)	Y-BOCS	Total OCD symptomatology; obsessive symptoms; compulsive symptoms	Score; specific obsessions and compulsions;	7 (GOOD)
Timpano et al. (2012), USA	Cross-sectional	Outpatients	OCD (526) OCD-BD (79)	NA	39.24 [17–92]* 39.5 [20–81]*	59.3% 64.6%	DSM-IV	Y-BOCS	Total OCD symptomatology; obsessive symptoms; compulsive symptoms	Score; Obsession subscore; Compulsion subscore	5 (FAIR)
Tukel et al. (2006), Turkey	Cross-sectional	Outpatients	OCD (91) OCD-BD (26)	Euthymic (100 %)	28.67 ±10.8 32.3 ± 14.3	59% 61.5%	DSM-IV (SCID)	Y-BOCS	Total OCD symptomatology; obsessive symptoms; compulsive symptoms	Score; Obsession subscore; Compulsion subscore; specific obsessions and compulsions;	7 (GOOD)
(Zutshi et al., 2007), India	Cross-sectional	Outpatients	OCD (78) OCD-BD (28)	Euthymic (100 %)	26.47 ±7.38 27.93 ±6.71	42% 25%	DSM-IV	Y-BOCS	Total OCD symptomatology; obsessive symptoms; compulsive symptoms	Score; Obsession subscore; Compulsion subscore; specific obsessions and compulsions;	7 (GOOD)

*Age range.

Notes: BD - Bipolar Disorder; **CY-BOCS** - Children's Yale–Brown Obsessive–Compulsive Scale; **DSM** - Diagnostic and Statistical Manual of Mental Disorders; **DY-BOCS** - Dimensional Yale-Brown obsessive-compulsive scale; **K-SADS** - Kiddie Schedule for Affective Disorders and Schizophrenia; **NOS** - Newcastle-Ottawa Scale; **OCD** - Obsessive-Compulsive Disorder; **OCSS** - Obsessive-Compulsive Symptom Survey; **SCID** - Structured Clinical Interview for DSM Disorders; **Y-BOCS** - Yale–Brown Obsessive–Compulsive Scale.

Table 2
Results of the meta-analyses in detail.

Outcome type	Studies, n	OCD-BD patients, n	OCD patients, n	SMD/ OR	95 % CI	p-value	95 % PI	I^2 (%)	tau^2	Q-test p-value
Obsessive-Compulsive symptomatology										
Total symptomatology	12	461	2492	−0.305	−0.663, 0.053	0.094	−0.908, 1.519	90.4	0.35	<0.001
Obsessive symptomatology	9	380	2416	−0.271	−0.737, 0.195	0.254	−1.152, 1.694	93.7	0.47	<0.001
Compulsive symptomatology	9	380	2416	−0.185	−0.534, 0.164	0.298	−0.851, 1.221	88.9	0.25	<0.001
Obsessions, number and type										
Number of obsessions, any	4	133	235	0.159	−0.443, 0.76	0.605	−1.112, 1.429	86.6	0.33	<0.001
Aggressive	11	398	1984	1.143	0.884, 1.478	0.306	0.884, 1.478	0	0	0.12
Contamination	9	280	1009	**0.711**	**0.532, 0.95**	**0.021**	**0.532, 0.95**	0	0	0.46
Sexual	9	280	1009	**1.765**	**1.025, 3.038**	**0.04**	0.483, 6.455	57.6	0.36	<0.001
Hoarding/saving	9	300	1599	1.462	0.907, 2.359	0.119	0.564, 3.789	37	0.18	0.11
Religious	9	280	1009	1.186	0.718, 1.96	0.505	0.349, 4.03	56.4	0.32	0.02
Symmetry/exactness	9	305	997	1.245	0.735, 2.11	0.415	0.314, 4.94	67.5	0.42	<0.001
Miscellaneous	8	303	1806	1.035	0.772, 1.389	0.817	0.772, 1.389	0	0	0.61
Somatic	7	218	874	0.943	0.632, 1.41	0.776	0.632, 1.41	0	0	0.75
Pathological doubt	3	79	162	0.756	0.267, 2.142	0.598	0.13, 04.383	63.5	0.52	0.07
Compulsions, number and type										
Number of compulsions, any	4	133	235	−0.164	−0.515, 0.186	0.359	−0.817, 0.488	61.6	0.08	0.05
Cleaning/washing	10	324	1103	0.697	0.481, 1.011	0.057	0.296, 1.644	44.5	0.16	0.06
Checking	8	248	948	0.863	0.577, 1.289	0.471	0.383, 1.942	39.7	0.13	0.12
Repeating rituals	7	192	661	1.233	0.462, 3.293	0.676	0.096, 15.87	84.3	1.45	<0.001
Counting	7	218	874	1.033	0.721, 1.481	0.857	0.721, 1.481	0	0	0.92
Ordering/arranging	7	232	723	1.042	0.615, 1.765	0.879	0.343, 3.163	51.7	0.25	0.03
Hoarding/collecting	8	226	718	1.25	0.557, 2.806	0.588	0.178, 8.796	64.8	0.82	<0.001
Miscellaneous	8	263	982	1.277	0.889, 1.835	0.186	0.646, 2.524	32.1	0.09	0.15

4. Discussion

The aim of this systematic review and meta-analysis was to examine the differences in the obsessive-compulsive symptomatology in people diagnosed with BD and OCD, compared with people diagnosed with OCD without BD. Overall, people with the comorbid condition were more likely to have experienced sexual obsessions than those without the comorbid condition during their lifetime, while they were less likely to have experienced contamination obsessions. No significant differences were observed with respect to other types of obsessions, types of compulsions, or severity of obsessive-compulsive symptomatology.

Sexual obsessions are repetitive, intrusive, and ego-dystonic thoughts about sexual orientation, infidelity, perversion, or sexual behavior in general, which may concern the self or others (Gordon, 2002). Their prevalence in OCD fluctuates between 20 and 30 % (Fernandez de la Cruz et al., 2013; Ruscio et al., 2010; Williams and Farris, 2011), with peaks reaching 50 % in some samples (Rady et al., 2013), although often they are poorly studied or explored in research and clinical settings (Real et al., 2013). Our results can be justified in several ways, including the obvious fact that sexual disinhibition is a common feature of manic and hypomanic episodes. Moreover, dysregulated impulsive behavior could serve as a crucial link between OCD and BD. Notably, individuals with OCD, particularly those grappling with sexual obsessions, exhibit heightened levels of impulsivity in comparison to those without such obsessions (Sahmelikoglu Onur et al., 2016). Some researchers suggest that sexual, religious, and aggressive obsessions may collectively represent a distinctive subtype of OCD, and this subtype appears to be closely tied to impulsive behaviors (Hasler et al., 2005). Furthermore, it is noteworthy that impulsivity holds significant relevance as both a state and trait aspect of BD. This is underscored by its well-documented neurobiological basis (Fico et al., 2020; Jiménez et al., 2014). Given these connections, it is plausible to consider sexual obsessions as potential symptoms that could help identify individuals with elevated impulsiveness, bridging the gap between OCD and BD. Our results find support in neuroimaging studies as well, with sexual obsessions associated with increased activation of specific brain regions, including the amygdala (Sevinc and Spreng, 2014). Interestingly, alterations in amygdala activation in response to emotional stimuli have also been documented in individuals with BD, leading to clinical heterogeneity (Kjaerstad et al., 2022; Njau et al., 2020; Phillips and Narendran, 2022; Xu et al., 2021). From a clinical point of view, it seems necessary to further investigate the presence of sexual obsessions to suspect comorbidity and provide personalized treatment strategies that take into account the risks associated with the use of SSRIs. Indeed, as mentioned before, the first-line pharmacological interventions for patients with OCD are the SSRIs (Stein et al., 2019), but their use in patients with BD should be considered with caution, especially in the absence of an adequate mood stabilization (Ghaemi et al., 2003; Pacchiarotti et al., 2013). Taken together with the fact that the presence of sexual obsessions has been associated with lower treatment response in some samples with OCD (Alonso et al., 2001), the presence of this symptomatology may guide the clinician to also consider second-line strategies, such as the use of second-generation antipsychotics (e.g., aripiprazole, risperidone) (Kellner, 2010), which have also demonstrated efficacy in BD (Cipriani et al., 2011; Kishi et al., 2021, 2022). However, despite the fact that the diagnosis of BD is not always obvious due to the challenges of obtaining an accurate history (Vieta et al., 2018), the potential delayed age of onset (Bolton et al., 2021), or the clinical heterogeneity (Lieberman et al., 2008), a single lifetime clinical symptom may not be sufficient to change the clinical management of patients this much, especially due to the transdiagnostic nature of these symptoms (Rasmussen and Parnas, 2022). For this reason, the best approach would be a thorough and systematic investigation of the clinical symptoms and features associated with BD once sexual obsessions have been identified in this population.

Contamination obsessions are characterized by a sense of being contaminated, soiled, infected, or endangered after direct or indirect contact with something perceived as impure, dirty, infectious, or harmful (Rachman, 2006). These obsessions are quite prevalent in OCD, affecting nearly half of this population (Markarian et al., 2010; Rasmussen and Eisen, 1992; Stein et al., 2019), and they are believed to be related to disgust sensitivity (Moretz and McKay, 2008). Our results

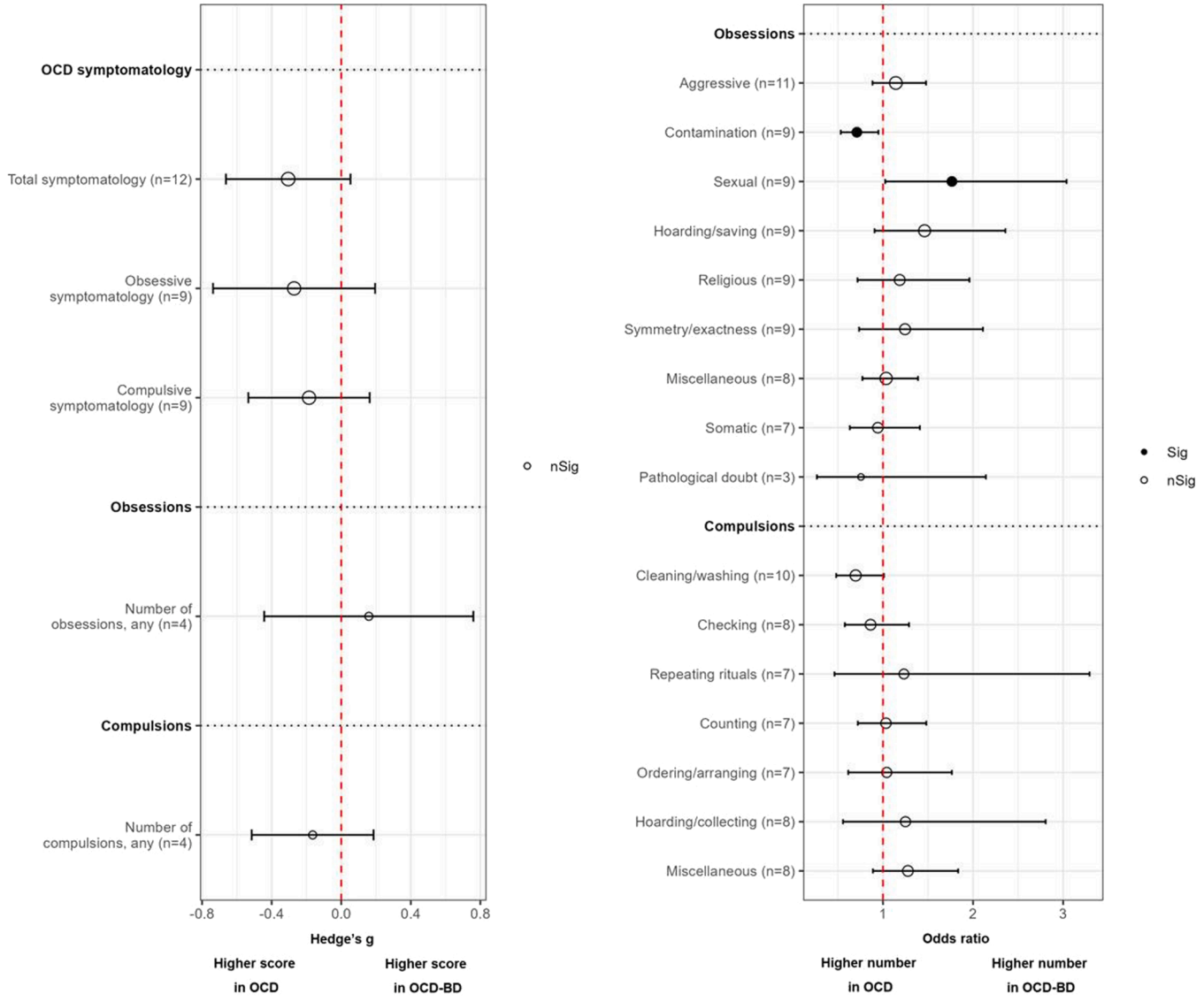

Fig. 2. Differences in obsessive-compulsive symptomatology (left), and lifetime frequency of specific obsessions and compulsions (right) between people with bipolar disorder comorbid with obsessive-compulsive disorder and people with obsessive-compulsive disorder. Overall results of the comparisons included in the meta-analysis. Legend: *BD*, Bipolar Disorder; *OCD*, Obsessive-Compulsive Disorder. Point size is proportional to the number of patients included in that specific comparison.

show that people with BD and OCD have a lower lifetime frequency of these obsessions compared to people with OCD without BD, suggesting that BD may be somewhat protective against this specific symptomatology. One possible explanation may be that BD patients pay less attention to disgust stimuli, making them less likely to develop contamination obsessions. Indeed, several studies have observed that BD patients are less accurate and attentive in recognizing (Branco et al., 2018; Hoertnagl et al., 2011; Soeiro-de-Souza et al., 2012) or matching (Bozikas et al., 2006) expressions of disgust, suggesting that such emotional cues may be less noticed by this population, despite conflicting evidence has been found on the matter. Therefore, to clarify whether altered disgust sensitivity can explain a different frequency of contamination obsessions in the comorbid OCD-BD population, studies primarily aimed at this purpose are needed.

No other significant differences were observed by our analyses regarding the type of obsessions or compulsions, or the severity of OCD symptomatology. The comorbidity of BD may characterize a slightly different clinical profile of OCD, and its main impact may be on the course of the illness and the frequency of occurrence of obsessive-compulsive symptoms, rather than on their intensity. Although OCD tends to be a chronic disorder in which the presence of symptomatology is almost constant, a phenotype characterized by the presence of periods of absent or reduced symptomatology, called episodic OCD, has been described (Kuehne et al., 2020; Pinto et al., 2006). Compared to people with chronic OCD, people with episodic OCD appear to have more lifetime BD comorbidity (Bramante et al., 2023), and at the same time, people diagnosed with both BD and OCD seem to have a more episodic course of OCD compared to people with OCD without BD (Mahasuar et al., 2011b; Perugi et al., 1997; Zutshi et al., 2007). BD type also seems to play a role: according to our meta-regressions, samples with a lower proportion of people diagnosed with BD-I were more likely to have more severe symptoms and a higher mean number of compulsions. It is possible that longer episode duration, more prominent anxiety symptomatology, or higher percentage of time spent in a depressive or sub-depressive state described in BD-II patients (Tondo et al., 2022), may account for the worsening of obsessive-compulsive symptomatology in this comorbid population. However, the role of affective symptomatology was not fully analyzed because only a subset of studies

reported this information, and most subjects were in remission. Based on the limited data available in this regard, a significant association emerged between the increased number of people with current (hypo) manic symptoms and the frequency of hoarding/collecting compulsions and the reason for this association may be found in the consequences of this affective symptomatology. For example, during a (hypo)manic episode, individuals may show decreased ability to concentrate, increased interest in activities, or overspending, which may result in a large number of purchases and possibly contribute to hoarding symptoms.

Finally, when only good-quality studies were considered, the results changed slightly. Differences in sexual obsessions did not reach significance, reinforcing the aforementioned heterogeneity of this construct. On the other hand, the significant difference observed for contamination obsessions remained and was strengthened by reduced levels of cleaning/washing compulsions in comorbid individuals, suggesting that the entire thought-action phenotype (i.e., contamination obsession-cleaning/washing compulsion) may be useful in distinguishing non-comorbid individuals from comorbid ones.

To the best of our knowledge, this is the first systematic review and meta-analysis comparing people diagnosed with both OCD and BD with people diagnosed with OCD without BD regarding obsessive-compulsive symptoms. The presence of obsessions represents a transdiagnostic entity in psychiatry. Therefore, clinicians should be aware that relying on the presence of a single lifetime symptom may not be sufficient for directing patient management. However, detecting the presence of sexual or contamination obsessions through a detailed interview could give us a slightly greater confidence in the management of each patient, allowing a more careful selection of the most appropriate treatment in the context of precision psychiatry (Arns et al., 2022; Fusar-Poli et al., 2022; Salagre and Vieta, 2021).

The present study comes with some limitations. First, the stability of our results was suboptimal, as they changed in significance after certain studies were removed from the analyses. However, GOSH plots did not allow us to identify clear outliers, and even after sensitivity analyses, the magnitude and direction of the estimate did not change much, suggesting the importance of a meta-analytic approach to clarify these associations. Second, most of the results, when reported, refer to populations in euthymia, limiting the generalizability of our findings to populations with current affective symptomatology. However, when possible, we conducted meta-regressions on both the percentage of patients in a particular affective state, and on affective symptomatology to address this point at least in part. Third, we focused on comparing OCD patients with and without BD, but the presence of other comorbidities in these populations is the rule rather than the exception, potentially affecting the symptoms we studied. However, among the many comorbidities that affect people with OCD, we attempted to control for lifetime diagnosis of MDD in meta-regressions because of the possible similarities between this diagnosis and BD. Fourth, the disparity of the samples is notable, with the numerosity of OCD-BD patients almost five times smaller than that of patients with OCD without BD. Although this may affect the power of our analyses, it is important to mention that this is due to the prevalence of the comorbidity, and thus the samples reflect the true proportion of these conditions. Fifth, individual studies report information on lifetime experience of specific obsessions and compulsions, which prevents us from knowing whether this symptomatology is still present or how it has evolved over time. Similarly, the cross-sectional nature of most of the included studies precludes us from drawing any causal conclusions. Sixth, five of the included studies did not report diagnosis through a (semi)structured interview. This may reduce the generalizability of our findings, as there may be low diagnostic reliability between studies due to different diagnostic approaches. Seventh, due to the paucity of available information, the type of drug treatment or its dosage could not be adequately controlled, although they may play a role in our outcome (De Prisco and Oliva, 2023; Ilzarbe and Vieta, 2023).

In conclusion, people with BD and OCD do not seem to differ from people with OCD without BD in obsessive-compulsive symptomatology, despite the differences in experiencing sexual and contamination obsessions. A more in-depth study of affective symptoms in larger samples might better delineate the differences that exist in this complex clinical phenotype.

Open practices statement

The datasets and the codes used for this research are available on request.

Role of the funding source

None

CRediT authorship contribution statement

Michele De Prisco: Visualization, Data curation, Conceptualization, Methodology, Formal analysis, Software, Writing – original draft. **Cristiana Tapoi:** Visualization, Data curation, Conceptualization, Methodology, Formal analysis, Software, Writing – original draft. **Vincenzo Oliva:** Data curation, Methodology, Formal analysis, Software, Writing – review & editing. **Chiara Possidente:** Data curation, Formal analysis, Writing – review & editing. **Robertas Strumila:** Data curation, Writing – review & editing. **Christine Takami Lageborn:** Data curation, Writing – review & editing. **Lorenzo Bracco:** Data curation, Writing – review & editing. **Nicolaja Girone:** Data curation, Writing – review & editing. **Monica Macellaro:** Data curation, Writing – review & editing. **Eduard Vieta:** Visualization, Conceptualization, Supervision, Writing – review & editing. **Giovanna Fico:** Visualization, Conceptualization, Supervision, Writing – review & editing.

Declaration of Competing Interest

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.euroneuro.2023.11.006.

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