TECHNICAL COMMENTARY

Obsessive-compulsive disorder

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Introduction

Obsessive-compulsive disorder involves persistent and intrusive thoughts (obsessions) and repetitive actions (compulsions). The DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) defines obsessions as recurrent and persistent thoughts, urges, or impulses that are experienced as intrusive and unwanted, with associated anxiety or distress. The individual attempts to suppress these obsessions by performing a compulsion; repetitive behaviours (e.g., hand washing, ordering, checking) or thoughts (e.g., praying, counting, repeating words). The obsessions or compulsions are time-consuming and can cause significant impairment in social, occupational, or other areas of functioning.

Related disorders include hoarding disorder, excoriation disorder (skin-picking), body dysmorphic disorder (obsessive focus on a perceived flaw in appearance) and trichotillomania (hair-pulling).

Method

We have included only systematic reviews (systematic literature search, detailed methodology with inclusion/exclusion criteria) published in full text, in English, from the year 2010 that report results separately for people with a diagnosis of bipolar or related disorders. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Hand searching reference lists of identified reviews was also conducted. When multiple copies of review topics were found, only the most recent and/or comprehensive review was included. Reviews with pooled data were prioritised for inclusion.

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist that describes a preferred way to present a meta-analysis[1]. Reviews with less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found six systematic reviews that met our inclusion criteria[3-8].

- Moderate quality evidence finds the lifetime prevalence of obsessive-compulsive

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disorder in people with bipolar disorder is around 11% compared to 2.5% in the general population. The current prevalence rate is also around 11% in people with bipolar disorder compared to 1.6% in the general population. The current prevalence during euthymia in people with bipolar disorder is around 7%. This represents a large increased risk of obsessive-compulsive disorder in people with bipolar disorder.

- Moderate quality evidence suggests the lifetime prevalence of obsessive-compulsive disorder in children and adolescents is around 17%. Adolescents with bipolar disorder showed higher rates of obsessive-compulsive disorder than children with bipolar disorder.
- Moderate quality evidence found mood stabilizers plus aripiprazole may be effective maintenance therapy for bipolar disorder and for treating obsessive-compulsive symptoms during manic episodes.
- Moderate to low quality evidence finds mood-stabilizers plus topiramate or memantine may relieve obsessive-compulsive symptoms during manic episodes.

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Amerio A, Maina G, Ghaemi SN

Updates in treating comorbid bipolar disorder and obsessive-compulsive disorder: A systematic review

Journal of Affective Disorders 2019; 256: 433-40

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Comparison	**Treatment of obsessive-compulsive disorder in people with bipolar disorder.**
Summary of evidence	**Moderate quality evidence (large sample, unable to assess precision, direct) suggests aripiprazole plus mood stabilisers may be effective maintenance therapy for bipolar disorder and for treating obsessive-compulsive symptoms during manic episodes.**
Obsessive-compulsive disorder treatment	
15 studies, N = 1,337 Authors report that 6/15 studies found aripiprazole plus mood stabilisers demonstrated to be effective maintenance therapy for bipolar disorder and for treating obsessive-compulsive symptoms during manic episodes.	
Consistency in results	Unable to assess; no measure of consistency is reported.
Precision in results	Unable to assess; no measure of precision is reported.
Directness of results	Direct

Ferentinos P, Preti A, Veroniki AA, Pitsalidis KG, Theofilidis AT, Antoniou A, Fountoulakis KN

Comorbidity of obsessive-compulsive disorder in bipolar spectrum disorders: Systematic review and meta-analysis of its prevalence

Journal of Affective Disorders 2020; 263: 193-208

View review abstract online

Comparison	**Lifetime and current prevalence of obsessive-compulsive disorder in people with bipolar disorder.**

Summary of evidence	**Moderate quality evidence (large samples, inconsistent, unable to assess precision, direct) suggests the lifetime prevalence of obsessive-compulsive disorder in people with bipolar disorder is around 11% compared to 2.5% in the general population. The current prevalence rate is also around 11% in people with bipolar disorder compared to 1.6% is the general population.**
Obsessive-compulsive disorder	
Lifetime prevalence: 39 studies, N = 8,205, 10.9%, 95%CI 7.8% to 14.4%, I^2 = 93% General population lifetime prevalence = 2.5% Current prevalence: 29 studies, N = 6,109, 11.2%, 95%CI 7.6% to 15.3%, I^2 = 91% General population current prevalence = 1.6% There were no significant differences in rates according to differences in samples (children/adolescents vs. mixed/adults), study setting (epidemiological or clinical), diagnostic criteria/procedures, gender, bipolar subtype or remission status.	
Consistency in results	Inconsistent
Precision in results	Unable to assess; not standardised measure.
Directness of results	Direct

Netto VM, Flores CA, Pallanti S

Pharmacological Treatment for Comorbid Bipolar Disorder and Obsessive-Compulsive Disorder in Adults

Journal of Psychiatric Practice 2020; 26: 383-93.

View review abstract online

Comparison	**Pharmaceutical treatment of obsessive-compulsive disorder in people with bipolar disorder.**
Summary of evidence	**Moderate to low quality evidence (very small sample, consistent, imprecise, direct) finds augmentation of mood-stabilizers with glutamate modulator agents (topiramate or memantine) for 4 months may favour full response of obsessive-compulsive symptoms in people with bipolar I disorder in a manic phase vs. placebo.**

Obsessive-compulsive disorder	
Augmentation of mood-stabilizers with glutamate modulator agents (topiramate or memantine) for 4 months may favour full response of obsessive-compulsive symptoms in people with bipolar I disorder in a manic phase vs. placebo; 2 RCTs, N = 71, RR = 2.62, 95%CI 1.45 to 4.74, I^2 = 0%	
Risks	There were no differences in adverse events between treatment and placebo groups.
Consistency in results	Consistent
Precision in results	Imprecise
Directness of results	Direct

Pavlova B, Perlis RH, Mantere O, Sellgren CM, Isometsa E, Mitchell PB, Alda M, Uher R

Prevalence of current anxiety disorders in people with bipolar disorder during euthymia: a meta-analysis

Psychological Medicine 2017; 47: 1107-15

View review abstract online

Comparison	**Current prevalence of obsessive-compulsive disorder in people with bipolar disorder during euthymia.**
Summary of evidence	**Moderate quality evidence (large samples, inconsistent, unable to assess precision, direct) suggests the current prevalence of obsessive-compulsive disorder in people with bipolar disorder during euthymia is around 7%.**
Obsessive-compulsive disorder	
Current prevalence: 10 studies, N = 2,193, 7%, 95%CI 0.4% to 10%	
Consistency in results	Authors report results are inconsistent.
Precision in results	Unable to assess; not standardised measure.
Directness of results	Direct

Saha S, Lim CCW, Cannon DL, Burton L, Bremner M, Cosgrove P, Huo YJ, McGrath J

Co-morbidity between mood and anxiety disorders: A systematic review and meta-analysis

Depression and Anxiety 2021; 38: 286-306

View review abstract online

Comparison	**Prevalence of obsessive-compulsive disorder in people with bipolar disorder vs. people without bipolar disorder.**
Summary of evidence	**Moderate quality evidence (unclear sample size, some inconsistency, imprecise, direct) finds a large, increased risk of obsessive-compulsive disorder in people with bipolar disorder compared to people without bipolar disorder.**
Obsessive-compulsive disorder	
Large increased risk of lifetime obsessive-compulsive disorder in people with bipolar disorder; 6 studies, N not reported, OR = 6.7, 95%CI 1.3 to 35.4, I^2 = 96.8% Adjusted OR = 8.4 *Large increased risk of obsessive-compulsive disorder over the last 1-12 months in people with bipolar disorder;* 4 studies, N not reported, OR = 7.0, 95%CI 3.0 to 16.1, I^2 = 17.8% Adjusted OR = 7.4 Adjusted for age, sex, race, and having another mental disorder.	
Consistency in results	Inconsistent for lifetime prevalence, consistent for period prevalence.
Precision in results	Imprecise
Directness of results	Direct

Yapici Eser H, Taskiran AS, Ertinmaz B, Mutluer T, Kilic O, Ozcan Morey A, Necef I, Yalcinay M, Ongur D

Anxiety Disorders Comorbidity in Pediatric Bipolar Disorder: A meta-analysis and meta-regression study

Acta Psychiatrica Scandinavica 2020; January 03

View review abstract online

Comparison	**Lifetime prevalence of obsessive-compulsive disorder in children (<12 years) and youth (13-18 years) with bipolar disorder.**
Summary of evidence	**Moderate quality evidence (large sample, inconsistent, unable to assess precision, direct) suggests the lifetime prevalence of obsessive-compulsive disorder is around 17%. Adolescents with bipolar disorder showed higher rates of obsessive-compulsive disorder than children with bipolar disorder (23.6% vs. 13.9%).**
Obsessive-compulsive disorder	
Lifetime prevalence: 23 studies, N = 2,363, 16.7%, 95%CI 11.4% to 23.8%, I^2 = 93% Adolescent-onset studies reported significantly greater rates of obsessive-compulsive disorder than childhood-onset studies (23.6% vs. 13.9%).	
Consistency in results	Inconsistent
Precision in results	Unable to assess; not standardised measure.
Directness of results	Direct

Explanation of acronyms

CI = confidence interval, I^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), N = number of participants, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), RR = risk ratio, vs. = versus

Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[9].

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect[9].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[10]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios measure the effect of an explanatory variable on the hazard or risk of an event.

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Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I^2 is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I^2 can be calculated from Q (chi-square) for the test of heterogeneity with the following formula[9];

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed[11].

‖ Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A versus B. Indirectness of population, comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention, comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-to-head comparisons of A and B.

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