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Course of illness in comorbid bipolar disorder and obsessive–compulsive disorder patients

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ABSTRACT

Psychiatric comorbidity is extremely common. One of the most common and difficult to manage comorbid conditions is the co-occurrence of bipolar disorder (BD) and obsessive compulsive disorder (OCD). We updated our recent systematic review searching the electronic databases MEDLINE, Embase, and PsycINFO to investigate course of illness in BD–OCD patients. We identified a total of 13 relevant papers which found that the majority of comorbid OCD cases appeared to be related to mood episodes. OC symptoms in comorbid patients appeared more often during depressive episodes, and comorbid BD and OCD cycled together, with OC symptoms often remitting during manic/hypomanic episodes.

1. Introduction

A diagnosis can be considered valid when one can differentiate it from other diagnoses. In a classic 1970 paper Robins and Guze described criteria to define the validity of a diagnostic construct of interest based on the availability of data on phenomenology, course of illness, heredity, biological markers, and treatment response (Robins and Guze, 1970).

Psychiatric comorbidity is extremely common in bipolar disorder (BD). More than half of BD patients have an additional diagnosis, one of the most difficult to manage being obsessive–compulsive disorder (OCD). In our recent meta-analysis, the pooled prevalence of OCD in BD was 17.0% (95% CI 12.7 to 22.4%), which was comparable to the results reported by the pooled prevalence of BD in OCD (18.35%, 95% CI 13.2 to 24.8%) (Amerio et al., 2015).

Although recent studies have investigated the co-occurrence of anxiety disorders and BD, the topic is insufficiently studied and the relationship between BD and OCD remains unclear (Amerio et al., 2014a; Tonna et al., 2015). What remains unclear is whether this high comorbidity represents the frequent occurrence of two independent diseases, or whether it represents the occurrence of symptoms of one kind (e.g., OCD symptoms) in a different disease (i.e., BD).

In agreement with Kraepelin's thought a psychiatric diagnosis is best established by its longitudinal course of illness, we updated our recent systematic review to investigate specifically the course of illness in BD–OCD patients.

2. Updated systematic review

Studies were identified by searching the electronic databases MEDLINE, Embase, and PsycINFO. We combined the search strategy of free text terms and exploded MESH headings for the topics of bipolar disorder, obsessive–compulsive disorder and treatment combined as following: (((((((("Bipolar Disorder"[Mesh]) OR Bipolar disorder) OR BD) OR Bipolar) OR Manic depressive disorder) OR Manic depressive) OR Manic)) AND ((((("Obsessive-Compulsive Disorder"[Mesh]) OR OCD) OR Obsessive-compulsive) OR Obsessive-compulsive disorder)). Studies published in English through November 15th, 2015 were included.

Thirteen studies were selected (Table 1). Higher rates of episodic OCD were reported in BD–OCD patients as compared to

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Table 1
Studies that met inclusion/exclusion criteria for systematic review.

References	Study design	Country	Study population	Diagnosis assessment	Results	Quality *
Goes et al. (2012)[1]	Cross-sectional study	USA	BD ($n=1416$, mean age = 42.0), first-degree relatives with BD ($n=850$)	DIGS; DSM-IV	Higher number of depressive episodes in OCD–BD patients vs. non-OCD–BD patients (19.7 vs. 10.3).	23/31
Issler et al. (2005)[2]	Case control study	Brazil	OCD–BD ($n=15$, mean age = 38.9 ± 10.7)	SCID; DSM-IV	Higher rate of chronic course of OCD in OCD–BD patients vs. non-OCD–BD patients (86.7% vs. 13.3%)[b]	14/31
Issler et al. (2010)[3]	Case control study	Brazil	BD ($n=30$, mean age: BD = 41.8 ± 10.5, OCD–BD = 38.9 ± 10.7)	SCID; DSM-IV	Higher number of depressive episodes in OCD-BD patients vs. non-OCD–BD patients (8.9 ± 4.2 vs. 4.1 ± 2.7). Higher rate of chronic course of BD in OCD–BD patients vs. non-OCD–BD patients (66.7% vs. 20%)[c]	17/31
Koyuncu et al. (2010)[4]	Case control study	Turkey	BD ($n=214$, mean age: BD = 34.8 ± 10.3, OCD–BD = 36.2 ± 15.9)	SCID; DSM-IV	Higher rate of chronic course of BD in OCD-BD patients vs. non-OCD-BD patients (17.1% vs. 0.0%)[c]	20/31
Mahasuar et al. (2011)[5]	Case control study	India	OCD ($n=91$, mean age: OCD = 29.36 ± 8.31, BD–OCD = 28.39 ± 7.10)	SCID; DSM-IV	Episodic course overrepresented in BD–OCD patients vs. patients without comorbidity (53% vs. 12%); higher rates of continuous (40% vs. 35%) or subclinical (32% vs. 6%) course in non-BD–OCD patients vs. BD–OCD patients[a,b]	19/31
Ozdemiroglu et al. (2015)[6]	Case control study	Turkey	BD ($n=48$, mean age = 42.3 ± 12.4), OCD ($n=61$, mean age = 37.7 ± 12.9), BD–OCD ($n=32$, mean age = 36.2 ± 12)	SCID; DSM-IV	A more episodic course of OCD, higher rates of rapid cycling, and the seasonality were found in BD–OCD patients. Depressive bipolar patients had a more severe OCD compared to euthymic patients[a]	23/31
Perugi et al. (1997)[7]	Case control study	Italy	OCD ($n=315$, mean age: BD–OCD = 32.8 ± 12.2, OCD = 32.5 ± 12.6)	NS; DSM-III-R	BD–OCD pt. were more inclined towards an episodic course of OCD symptoms vs. non-BD–OCD patients (42.6% vs. 26.9%)[a]	22/31
Perugi et al. (1998)[8]	Case control study	Italy	OCD ($n=135$, mean age = 38.4 ± 13.3)	NS; DSM-III-R	Statistically non-significant trends of higher rate of episodic OCD course in OCD patients with comorbid BD-II vs. patients without comorbidity[a]	21/31
Perugi et al. (2002)[9]	Case control study	Italy	OCD-MDE (n = 68, mean age = 34.2 ± 12.5); BD–OCD (n = 38, mean age = 35.9 ± 12.2)	SCID; DSM-IV	Higher rate of episodic course of OCD in BD–OCD patients vs. non-BD–OCD patients (52.6% vs. 16.7%)[a]	20/31
Strakowski et al. (1998)[10]	Cross-sectional study	USA	BD, manic or mixed with psychosis ($n=77$, mean age = 25 ± 6)	SCID; DSM-III-R	BD and OCD cycled together in 44% of BD–OCD patients followed for 12 months after a first hospitalization	22/31
Tukel et al. (2006)[11]	Case control study	Turkey	OCD ($n=115$, age >18)	SCID; DSM-IV	Higher number of BD–OCD patients with an episodic course of OCD vs. non-BD–OCD patients (42.3% vs. 10.9%)[a]	21/31
Tukel et al. (2007)[12]	Case control study	Turkey	OCD ($n=128$, mean age = 29.3 ± 10.8)	SCID; DSM-IV	Higher frequency of BD in patients with episodic OCD than in patients with chronic OCD (20.8% vs. 3.8%)[a]	21/31
Zutshi et al. (2007)[13]	Case control study	India	OCD ($n=106$, mean age: BD–OCD = 27.93 ± 6.71, OCD = 26.47 ± 7.38)	SCID; DSM-IV	Higher rate of episodic course of OCD in BD–OCD patients vs. non-BD–OCD patients (75% vs. 3%); higher rate of chronic course of OCD in non-BD–OCD patients vs. patients with comorbidity (97% vs. 14%). Most BD–OCD patients (78%) either had OCD confined exclusively to depressive episodes or reported worsening of OCD during depression. Improvement in OC symptoms was noted in 64% patients during manic/hypomanic episodes[a,b]	20/31

BD: bipolar disorder; OCD: obsessive–compulsive disorder; DSM: Diagnostic and Statistical Manual of Mental Disorders; SCID: Structured Clinical Interview; DIGS: Diagnostic Instrument for Genetic Studies; NS: Not specified; Vs.: versus.

* Checklist for measuring study quality developed by Downs and Black.

[a] Episodic OCD: at least one circumscribed symptom-free interval (six months) was present.

[b] Chronic OCD: if symptoms persisted for most of the course, causing significant distress and impairment in functioning.

[c] Chronic BD: if all criteria for a major mood episode were met continuously for at least two years. Differences statistically significant ($p < 0.05$).

[1] Goes, F.S., Mccusker, M.G., Bienvenu, O.J., et al., 2012. Co-morbid anxiety disorders in bipolar disorder and major depression: familial aggregation and clinical characteristics of co-morbid panic disorder, social phobia, specific phobia and obsessive–compulsive disorder. Psychol. Med. 42(7), 1449–1459.

[2] Koyuncu, A., Tukel, R., Ozyildirim, I., et al., 2010. Impact of obsessive–compulsive disorder comorbidity on the sociodemographic and clinical features of patients with bipolar disorder. Compr. Psychiatry 51(3), 293–297.

[3] Issler, C.K., Amaral, J.A., Tamada, R.S., et al., 2005. Clinical expression of obsessive–compulsive disorder in women with bipolar disorder. Revista brasileira de psiquiatria (Sao Paulo, Brazil: 1999) 27(2), 139–142.

[4] Issler, C.K., Monkul, E.S., De Mello Siqueira Amaral, J.A., et al., 2010. Bipolar disorder and comorbid obsessive–compulsive disorder is associated with higher rates of anxiety and impulse control disorders. Acta Neuropsychiatrica 22(2), 81–86.

[5] Mahasuar, R., Janardhan Reddy, Y.C., Math, S.B., 2011. Obsessive–compulsive disorder with and without bipolar disorder. Psychiatry Clin. Neurosci. 65(5), 423–433.

[6] Ozdemiroglu, F., Sevincok, L., Sen, G., et al., 2015. Comorbid obsessive–compulsive disorder with bipolar disorder: A distinct form? Psychiatry Res. [Epub ahead of print].

[7] Perugi, G., Akiskal, H.S., Pfanner, C. et al., 1997. The clinical impact of bipolar and unipolar affective comorbidity on obsessive–compulsive disorder. J. Affect. Disord. 46(1), 15–23.

[8] Perugi, G., Akiskal, H.S., Ramacciotti, S., et al., 1999. Depressive comorbidity of panic, social phobic, and obsessive–compulsive disorders re-examined: is there a bipolar II connection? J. Psychiatr. Res. 33(1), 53–61.

[9] Perugi, G., Toni, C., Frare, F., et al., 2002. Obsessive–compulsive-bipolar comorbidity: a systematic exploration of clinical features and treatment outcome. J. Clin. Psychiatry 63(12), 1129–1134.

[10] Strakowski, S.M., Sax, K.W., Mcelroy, S.L., et al., 1998. Course of psychiatric and substance abuse syndromes co-occurring with bipolar disorder after a first psychiatric hospitalization. J. Clin. Psychiatry 59(9), 465–471.

[11] Tukel, R., Meteris, H., Koyuncu, A., et al., 2006. The clinical impact of mood disorder comorbidity on obsessive–compulsive disorder. Eur. Arch. Psychiatry Clin. Neurosci. 256(4), 240–245.

[12] Tukel, R., Oflaz, S.B., Ozyildirim, I., et al., 2007. Comparison of clinical characteristics in episodic and chronic obsessive–compulsive disorder. Depress. Anxiety 24(4), 251–255.

[13] Zutshi, A., Kamath, P., Reddy, Y.C., 2007. Bipolar and nonbipolar obsessive–compulsive disorder: a clinical exploration. Compr. Psychiatry 48(3), 245–251.

patients without comorbidity. The only study that found a more profound chronic course of OCD in OCD-BD patients was conducted in a small group of 15 women mainly with BD-I. Two studies conducted in BD patients reported higher rates of chronic course of BD in OCD-BD patients versus non-comorbid patients. Most BD-–OCD subjects either had OCD confined exclusively to depressive episodes or reported worsening of OCD during depression; in particular, one report showed that in 44% of BD–OCD patients BD and OCD cycled together. When assessed, the total number of depressive episodes was higher in patients with OCD-BD comorbidity than in BD alone.

3. Limitations

The main limitation of this updated systematic review is linked to the study design and analysis strategy of the included studies, as documented in the quality assessment scale used. Most studies are observational and based on retrospective assessments. Small sample size and enrolment of subjects mainly from BD–OCD outpatient units may limit generalizability of these results.

The use of retrospective assessment scales with low sensitivity in discriminating true ego-dystonic obsessions from depressive ruminations may have biased results towards an overestimation of obsessive symptom prevalence. In addition, patients included in the review were mainly recruited from specialized BD and OCD outpatient units; this might have introduced selection bias and limited the generalizability of findings to the community, where such patients tend to be less refractory.

4. Conclusions

Results from this review support the view that the majority of cases of comorbid BD–OCD are, in fact, BD cases. Considering course of illness as a key diagnostic validator, especially among patients with a primary diagnosis of BD, the majority of comorbid OCD cases appeared to be related to mood episodes. OC symptoms in comorbid patients appeared more often – and sometimes exclusively – during depressive episodes, and comorbid BD and OCD cycled together, with OC symptoms often remitting during manic/hypomanic episodes.

Comorbid BD–OCD course of illness would explain why OCD and BD symptoms respond to adequate mood stabilizer treatment (Amerio et al., 2014b). Only in a minority of comorbid patients with persistent OCD, despite improvement in mood episodes, addition of low doses of antidepressants could be considered while strictly monitoring emerging symptoms of mania or mixed states.

These results would confirm the hypothesis of Mayer-Gross and colleagues reported in a standard 1969 psychiatry textbook:

> These people (BD–OCD patients) who, in time of health, show no noteworthy obsessional traits, but who have phases in which compulsive symptoms appear out of the blue and rapidly mount up to complete incapacitation... Nevertheless these illnesses remit and relapse in very much the same way as cyclothymic illnesses, may show just as much regularity of timing, and are probably to be included, from the aetiological point of view, in the manic-depressive disorders (Mayer-Gross et al., 1969).

Further original studies are needed to clarify BD–OCD comorbidity. In particular, studies addressing neurobiological substrates are essential to illuminate pathogenetic mechanisms that underlie comorbid BD–OCD.

Conflict of interest statement

Dr. Amerio, Dr. Tonna, Dr. Odone, and Dr. Stubbs report no conflicts of interest. Dr. Ghaemi has provided research consulting to Sunovion and Pfizer, and has obtained a research grant from Takeda Pharmaceuticals. Neither he nor his family hold equity positions in pharmaceutical corporations.

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Authors' contributions

Authors AA, MT, AO, and BS designed the study and wrote the protocol. Studies were identified and independently reviewed for eligibility by two authors (AA, AO) in a two-step based process. Data were extracted by one author (AA) and supervized by a second author (SNG) using an ad-hoc developed data extraction spreadsheet. The same authors who performed data extraction (AA, SNG) independently assessed the quality of selected studies using the checklist developed by Downs and Black both for randomized and non-randomized studies. AA, MT, AO, and BS have been involved in drafting the manuscript and SNG revised it critically. SNG has given final approval of the version to be published. All authors read and approved the final manuscript.

References

Amerio, A., Odone, A., Marchesi, C., et al., 2014a. Do antidepressant-induced manic episodes in obsessive–compulsive disorder patients represent the clinical expression of an underlying bipolarity? Aust. N. Z. J. Psychiatry 48, 957.

Amerio, A., Odone, A., Marchesi, C., et al., 2014b. Treatment of comorbid bipolar disorder and obsessive–compulsive disorder: a systematic review. J. Affect. Disord. 166, 258–263.

Amerio, A., Stubbs, B., Odone, A., et al., 2015. The prevalence and predictors of comorbid bipolar disorder and obsessive–compulsive disorder: a systematic review and meta-analysis. J. Affect. Disord. 186, 99–109.

Mayer-Gross, W., Slater, E., Roth, M., 1969. Clinical Psychiatry, Third ed. Elsevier Health Sciences, London.

Robins, E., Guze, S.B., 1970. Establishment of diagnostic validity in psychiatric illness: its application to schizophrenia. Am. J. Psychiatry 126 (7), 983–987.

Tonna, M., Amerio, A., Ottoni, R., et al., 2015. The clinical meaning of obsessive–compulsive symptoms in bipolar disorder and schizophrenia. Aust. N. Z. J. Psychiatry 49, 578–579.