Bipolar disorder and its comorbidities between Feinstein and the Diagnostic and Statistical Manual of Mental Disorders

Andrea Amerio^{1,2}, Anna Odone³, Matteo Tonna⁴, Brendon Stubbs⁵ and S Nassir Ghaemi^{2,6}

¹Department of Clinical and Experimental Medicine, University of Parma, Parma, Italy

²Mood Disorders Program, Tufts Medical Center, Boston, MA, USA

³Unit of Public Health, Department of Biomedical, Biotechnological and Translational Sciences, University of Parma, Parma, Italy

⁴Department of Mental Health, Local Health Service, Parma, Italy

⁵Institute of Psychiatry, Kings College London, London, UK

⁶Department of Psychiatry and Pharmacology, Tufts University Medical School, Boston, MA, USA

Corresponding author:

Andrea Amerio, Department of Clinical and Experimental Medicine, University of Parma, c/o Ospedale Maggiore, Viale A. Gramsci 14, 43126 Parma, Italy.

Email: andrea.amerio@studenti.unipr.it

DOI: 10.1177/0004867415610201

To the Editor

In a classic 1970 publication, the famous epidemiologist Alvan R. Feinstein defined *comorbidity* in relation to a specific index condition, as 'any distinct additional entity that has existed or may occur during the clinical course of a patient who has the index disease under study' (Maj, 2005). In Feinstein's formulation, the implication was that a completely different and independent disease occurred at the same time as another disease. These two diseases co-occurred, more often than not, randomly.

On the contrary, the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) explicitly produces overlapping clinical criteria for many diagnoses, especially mood and anxiety disorders, guaranteeing comorbidity in quite a different sense than in the medical

meaning of the term as co-occurrence of independent diseases (Maj, 2005). Using DSM definition, it is unclear whether concomitant diagnoses actually reflect the presence of distinct clinical entities or refer to multiple manifestations of a single clinical entity.

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) (Amerio et al., 2014a; Amerio et al., 2014b). In our recent meta-analysis, the pooled prevalence of OCD in BD was 17.0%, which was comparable to the results reported by the pooled prevalence of BD in OCD (18.35%) (Amerio 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 in a different disease.

According to Feinstein's definition, 'true' OCD comorbid with BD would represent the random co-occurrence of two independent diseases, estimated by multiplication of prevalence rates, which are about 1% for each condition, producing a very low expected true comorbidity of 0.1% in the general population.

In agreement with Kraepelin's thought, a psychiatric diagnosis is best established by its longitudinal course of illness; the evidence so far supports the view that the majority of comorbid OCD cases appeared to be related to mood episodes (Amerio et al., 2014a). Therefore, only a substantial minority of comorbid BD-OCD may represent 'true' OCD independent of BD with obsessive-compulsive (OC) symptoms that improve or worsen during mood episodes without being related to these.

These results would confirm the hypothesis of Mayer-Gross et al. reported in a standard 1969 psychiatry textbook (Clinical Psychiatry, 1969):

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.

Acknowledgements

A.A., A.O. and M.T. designed the study and wrote the protocol. A.A., A.O. and B.S. were involved in drafting the manuscript, and S.N.G. revised it critically. S.N.G. has given final approval of the version to be published. All authors read and approved the final manuscript.

Declaration of interest

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Drs Amerio, Odone, Tonna and Stubbs report no conflicts of interest. Dr Ghaemi has provided research consulting to Sunovion and Pfizer. Neither he nor his family holds equity positions in pharmaceutical corporations.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Dr Ghaemi has obtained a research grant from Takeda Pharmaceuticals.

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? *Australian and New Zealand Journal of Psychiatry* 48: 957–963.
- Amerio A, Odone A, Marchesi C, et al. (2014b) Treatment of comorbid bipolar disorder and obsessive-compulsive disorder: A systematic review. *Journal of Affective Disorders* 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. *Journal of Affective Disorders* 186: 99–109.
- Maj M (2005) 'Psychiatric comorbidity': An artefact of current diagnostic systems? *The British Journal of Psychiatry* 186: 182–184.
- Mayer-Gross W, Slater E and Roth M (1969) *Clinical Psychiatry*, 3rd Edition. London: Elsevier Health Sciences.