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Prevalence and clinical features associated to bipolar disorder–migraine comorbidity: a systematic review

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Abstract

Background: The prevalence and clinical features associated with bipolar disorders (BDs)–migraine comorbidity have been reported inconsistently across different studies, therefore warranting a systematic review on the matter.
Methods: A systematic review was conducted in accordance with the PRISMA statement searching major electronic databases for documents indexed between January, 2000 and July, 2014. Eligible studies were those including quantitative data on prevalence rates and clinical features associated to BD–migraine comorbidity; case reports excluded. Three authors independently conducted searches, quality assessment of the studies and data extraction.
Results: Several cross-sectional studies, and a handful of retrospective follow-up studies or non-systematic reviews assessed the prevalence and/or the clinical correlates of migraine–BD comorbidity. High prevalence rates and a significant burden of BD–migraine comorbidity were common findings, particularly in case of BD-II women (point-prevalence rates up to 77%), migraine with aura (up to 53%) and/or cyclothymic temperament (up to 45% of the cases).
Limitations: Some of the biases encountered in a few studies accounted by the present review may nonetheless have hampered the generalizability of the overall conclusions drawn herein.
Conclusions: BD–migraine comorbidity may comprise of a sub-phenotype of BDs requiring patient-tailored therapeutic interventions to achieve an optimal outcome. Specifically, additional studies including longitudinal follow-up studies are aimed in order to shed further light on the actual prevalence rates and clinical features associated to BD–migraine comorbidity, with a special emphasis towards the clinically suggestive potential connection between mixed features, bipolar depression, migraine, and increased risk for suicidality. PROSPERO registration number: CRD42014009335.

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1. Introduction

According to the *International Classification of Headache Disorders, 2nd edition* (*ICHD-2*), migraine refers to different phenotypes having in common a low threshold to the development of headache among migraineurs, usually being characterized for a recurring pattern, frequent free-interval, and usually provoked by stereotyped triggers [1]. Notwithstanding, a conclusive definition of migraine remains elusive, especially due to the heterogeneity of some of the frequently associated neurological and psychiatric comorbidities. Specifically, concerning psychiatric comorbidities, several large-scale population-based studies have confirmed clinicians' longstanding suspicions: mood (and Anxiety) disturbances are more prevalent in migraineurs vs. the general population [2]. Much research involving migraine and mood disorders, including prospective, large-scale, population-based studies, has focused on depression, yet a three-fold increase in migraine prevalence in patients with bipolar disorders (BDs) has been documented as well [3]. Specifically, treatment-seeking patients with migraine, and tension-type headache [4] exhibit psychiatric comorbidity (including BD) at rates disproportionately higher than individuals with no history of recurrent migraine [5–9]. However, the actual rates of BD among migraine patients and related clinical features have been reportedly inconsistent, especially when looking at peculiar features such as bipolar subtype, gender, and age or illness severity, at least in comparison with migraine–major depressive disorder (MDD) comorbidity, wherein rates have been documented to range between 3.8 and 57% compared with an average general population lifetime rate of 16% [10–12], or to comorbid generalized anxiety disorder or panic disorder, both found to have higher prevalence rates of migraine comorbidity compared to the general population (>50 vs. 27%) [2].

The purpose of the present systematic review is to examine the prevalence rates of migraine–BD comorbidity and the clinical features associated to both migraine in course of BD and BD in course of migraine.

2. Material and methods

Aimed at achieving a high standard of reporting, we followed the procedures indicated by the 2009 update of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (http://www.prisma-statement.org/) [13]. The protocol of the present systematic review is available through PROSPERO (http://www.crd.york.ac.uk/PROSPERO/), where it was assigned the following registration number: CRD42014009335.

2.1. Eligibility criteria

We limited our search to those records including adult subjects with BD, published in peer-reviewed journals. Limits activated were: species: humans, language: English, all adult: 19+, publication date: from January 1, 2000 to July 25, 2014. Such criteria were adopted following clinical considerations, aimed at providing quality consistency among the studies, yet screening as many sources as possible. Specifically, disregard of contributes indexed before year 2000 essentially followed "diagnostic reliability" considerations. In fact, it was in the 1980 US release of the *DSM-III* [14] that the term "bipolar disorder" replaced the older term "manic depressive disorder". The new term, "bipolar disorder" reflected the defining feature of mood polarity rather than simply pointing to the consequences of that polarity: mania and depression, also indicating the distinction between adult and pediatric bipolar disorder diagnoses for the first time. Similarly, the older diagnostic criteria for "migraine" were largely inconsistent with the most recently introduced and broadly adopted ones. Essential contributes published before year 2000 have nonetheless been acknowledged through the text for consistency issues [6,15].

2.1.1. Information sources and search strategy

Sources of information included the following databases: PubMed/Medline, Scopus, PsycLit, PsycInfo, Embase, and Cochrane library. Contact with study authors was attempted when needed, leading to the identification on an additional document [16]. The following key words or their combination were used in the search strategy: "*migraine* AND *bipolar disorders*" either in the title and abstract (or in the key words where specified). The adopted PubMed string was: (migraine [Title/Abstract]) AND bipolar disorder[Title/Abstract]) AND ("2000"[Date – Publication] : "2014"[Date – Publication]).

2.2. Study selection

Included papers were those reporting epidemiological data about the comorbidity between migraine and BD (and *vice versa*), with no restriction on etiology or type. Papers covering cases of migraine–BD comorbidity associated with additional disorders (either psychiatric, neurological [including migraine due to epilepsy, Tourette's syndrome or schizophrenia] or to other somatic disorders/diseases) were also evaluated wherever available. When a title and/or an abstract appeared suggestive for inclusion, the full text reprint was obtained and examined to assess its relevance according to our inclusion/exclusion criteria. Excluded papers were case reports, papers not including BD migraine co-occurring cases, those merely focusing on neurobiological, genetic or pharmacological aspects of either migraine or BD; including only children or adolescents; or without an accurate description about the diagnostic definitions of either migraine and BD.

2.3. Data collection process

Three authors (MF, LI, and CDP) conducted a two-step literature search, examining all titles and abstracts, accessing the full texts of potentially relevant papers. Upon data