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Does Mood Disorder Questionnaire identify sub-threshold bipolarity? Evidence studying worsening of quality of life

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ABSTRACT

Objective: It is debated whether the Mood Disorder Questionnaire (MDQ) can generate false positives by screening other disorders as bipolar, or identify sub-threshold bipolarity. The aim is to verify if Quality of Life (QoL) impairment in MQD positives in the community is due to MDQ positivity itself, or to psychiatric diagnosis associated with MDQ positivity (supporting the former hypothesis).
Method: Community survey. Sample randomized after stratification of the adult population in the records of seven Italian regions. Tools: MDQ; Short Form Health Survey (SF-12); semi-structured clinical interview carried out by clinicians.
Results: Positives at MDQ show worsening QoL with an attributable burden of 2.8 ± 1.8 lower than in MDD (5.6 ± 3.6, $p < 0.001$) or Eating Disorders (4.4 ± 6.6, $p < 0.03$) and similar to Panic Disorder (2.9 ± 0.9, $p = 0.44$). The burden is lower in the middle-aged (25–59 years) than in the young (18–24) (4.65 ± 4.5 vs 2.58 ± 2.0, $p = 0.007$) or in the elderly (≥ 60) (4.12 ± 3.2; $p = 0.024$). In the elderly the burden is independent from comorbid psychiatric disorders.
Limitations: This is a preliminary study based on one survey not designed to test this specific hypothesis, thus its results have a heuristic value only.
Conclusions: The worsening of QoL due to positivity at MDQ is largely independent from comorbid conditions, supporting the hypothesis that MDQ positivity identifies a specific area of suffering that is "subthreshold" to the psychiatric diagnosis, and relevant for public health.

1. Introduction

The introduction of screening questionnaires for Bipolar Disorders in epidemiology – like the Mood Disorder Questionnaire (MDQ) (Hirschfeld et al., 2000) and the Hypomania Check List 32 (HCL-32) (Angst et al., 2010) – has enhanced research in the field of epidemiology of bipolar disorders. Several community surveys were carried out under this method in different countries in the past two decades: a study in the USA using the Mood Disorder Questionnaire found a slightly lower than 4% prevalence of positivity at the screening (lifetime) (Hirschfeld et al., 2003); in Australia prevalence was 2.5% with the same instrument (Fisher et al., 2007); 3% in Italy (Carta et al., 2012a,b) and 3.6% in France (Carta et al., 2013).

The publication of these data was followed by a heated debate; some researchers wrote that these instruments have low accuracy, because they generate false positives (Zimmerman et al., 2009) and consequently the high prevalence reported may be an artifact. Others defended the results on the basis that screening "positives"

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were homogeneous with Bipolar ones in factors such as: similar risk by gender, risk in young age, high level of subjective distress, low social functioning, comorbidity, low employment rate, substance abuse, high recourse to health care resources, high rate of use of stabilizers and antidepressants, risk of suicide attempts, high recurrence rate of depressive episodes (Carta et al., 2013). If none of these components alone may be considered "pathognomonic" of bipolar disorder, the co-occurrence of all the factors seems to identify "cases" worth considering in the bipolar spectrum, even though they are probably less severe than those fulfilling the full criteria of the current classification systems (Carta and Angst, 2005; Carta et al., 2013).

Another point of view is that atypical depression, borderline personality disorder and bipolar II disorder overlap manifestations of a common cyclothymic diathesis (Perugi et al., 2011). Therefore positivity at MDQ could identify a condition of vulnerability to mania that is a common feature not of the bipolar spectrum as described earlier, but of a spectrum that would include all these conditions (atypical depression, borderline personality disorder and bipolar II disorder) and therefore also of a pre-clinical condition (a milder form not yet defined in a disturbance) common to these conditions (Perugi et al., 2011).

In this framework some useful elements could arise by determining whether the impairment found in positives at MDQ can be attributed to the condition itself (positivity at MDQ) or to psychiatric disorders associated with it. If it were really proved that the typical impairment of MDQ positivity occurs regardless of comorbid conditions, this would strengthen the hypothesis that the positivity at MDQ identifies a specific condition and therefore also the so-called false positives (who are positive at MDQ without any associated psychiatric diagnosis) deserve clinical and public health attention.

The subjective perception of quality of life is a construct of well-known relevance today and it is adopted as a measure of outcome in diseases having a strong impact on the daily life of patients (Mantovani et al., 1996a, 1996b; Mura et al., 2012). It is believed that Bipolar Disorders deeply compromise the quality of life of BD patients; in fact an extensive review has found QoL significantly worsened in BD patients and the presence of comorbid conditions, so frequent in Bipolar Disorders, further decreases the QoL of BD patients (IsHak et al., 2012).

So far, the issue of QoL has not been extensively studied in MDQ positives. In a Canadian survey on primary care attenders, out of the total of 1304 patients completing the survey, 27.9% screened positive at MDQ (the rate of MDQ positives is obviously higher than those found in the community surveys mentioned before as this refers to primary care); positives were found significantly associated with depression, anxiety, substance use, attention deficit hyperactivity disorder, family history of bipolar disorder, suicide attempts, work or school productivity, and social and family functioning (Chiu and Chokka, 2011). Health-related quality of life measured by SF-12 was found significantly worse in subjects who screened positive (Chiu and Chokka, 2011). In a study involving patients with epilepsy, MDQ+ patients (10.1%) showed worse QoL that was associated with work, social, and family life disruptions as against the negatives at screening (Lau et al., 2012).

In two previous case-control studies on Mood Disorders in Wilson's Disease (Carta et al., 2012b) and Multiple Sclerosis (Carta et al., 2014a, b), MDQ positivity resulted as a determinant in the worsening of Quality of Life.

1.1. Aims of the study

The aim of this study is to measure the burden that may be attributed to positivity at MDQ in a community sample, and how factors such as age, gender and co-morbidity with mood, anxiety or eating disorders can interact with MDQ positivity in influencing the perception of the quality of life. The study will aim to determine whether positivity at MDQ "in itself" is associated with an impairment of quality of life (supporting the hypothesis that MDQ positivity identifies a spectrum of disorders of relevance even if subthreshold in respect to psychiatric diagnosis) or if such impairment is only due to the psychiatric illness expected to be more frequent in MDQ positivity.

A secondary goal will be to compare the effect of MDQ on the quality of life of the people in the community to that of subjects with other psychiatric diseases measured in the same nationwide surveys.

2. Methods

2.1. Sample

Data were drawn from a data bank of an epidemiologic study conducted with the main objective to measure the use of drugs for mood disorders in Italy (Carta et al., 2010, 2012b). As explained in detail in the previously published papers, a total of 3398 subjects from seven centers were interviewed. These locations were chosen for their wide variations in socio-economic variables (for instance: low and high mean income and rural/urban centers) and geographic distribution (north, center and south of Italy). From the original sample, the interviewees not giving all the answers to SF-12 items or to any other of the variables taken in account for this study (like comorbidity) were deleted. The remaining sample was made up of 2362 participants distributed as follows: 56.8% females and 43.2% males. The sample of this research did not differ from the original sample in terms of distribution by gender, age, and geographic distribution.

2.2. Study tools

The following tools were adopted for the survey:

1. An ad-hoc form to assess basic demographic data—a previously validated tool (Carta et al., 2010). Specifically, age was treated as a continuous variable and gender was coded as follows: 0—men and 1—women.
2. To ascertain comorbidity with DSM-IV mood (including bipolar I, II and cyclothymic disorder), anxiety and eating disorders (plus binge eating disorder) the "Advanced Neuropsychiatric Tools and Assessment Schedule" (ANTAS) has been adopted. This is a computerized semi-Structured Clinical Interview partially derived from the Structured clinical interview for DSM-IV axis I disorders, research version, non-patient edition (SCID-I/NP) (First et al., 1997); it was administered by clinicians (medical doctors or psychologists). A reliability study previously published found a mean k of 0.85 between the DSM-IV diagnoses derived from SCID and from ANTAS (Carta et al., 2010). The variable related to the presence of comorbidity was coded as follows: 0—absence, and 1—presence.
3. The Mood Disorder Questionnaire (MDQ) (Hirschfeld et al., 2000), Italian version (Hardoy et al., 2005), a screening tool for the assessment of bipolar spectrum disorders. The cut-off for positivity was set at the score ≥ 7 according to validation studies (Hardoy et al., 2005; Carta et al., 2010). A binary variable was created to identify patients with and without a diagnosis of bipolar disorder: 0—negative and 1—positive.
4. The perception of quality of life has been measured by means of the Short Form Health Survey (SF-12) (Ware et al., 1996). The SF-12 takes into consideration the following dimensions: physical activity; limitations on role or activities due to physical health; emotional state, pain, self-evaluation of general health, vitality, social activity and mental health. The period of