Ref: JAD\_2016\_1186

Title: The Difficult Lives of Individuals with Bipolar Disorder: Predictors of Functional Outcome and Implications for Treatment

ABSTRACT:

Background: Most longitudinal or treatment studies in bipolar disorder have used symptomatic or syndromal status as the primary outcome variable. More recently, psychosocial functioning has been highlighted as a key domain of outcome. Patients with bipolar disorder appear to be impaired in all functional domains, although the factors that cause impairment have not been clearly specified. Methods: This paper reviews the literature on functional impairment and the factors that underlie the variability in functioning among patients with bipolar disorder. Results and Discussion: Functional recovery following a mood episode consistently lags behind symptomatic and syndromal recovery. Longer term functional impairment is only partly explained by the number of manic/hypomanic episodes. Depression (including subsyndromal states) and persistent neurocognitive impairment are the strongest correlates of functional impairment in bipolar disorder. Few studies have examined potential treatments to combat these impairments. Possible treatment options include: more aggressive treatment of subthreshold depressive states, pharmacotherapies that target cognition such as stimulants, and adjunctive psychotherapies including cognitive remediation.

**Comment:** The authors review the literature on functional impairment and the factors that underlie the variability in functioning among patients with BD. I am glad the authors addressed and reviewed this field as too few papers integrate functional measures (such as quality of life or global functioning in daily activities) when assessing the effectiveness of treatments or the quality of remission. The primary limitation of this review is the narrative approach, e.g. a systematic/meta-analysis would have provided a more comprehensive and objective “understanding” of the state of the literature and potential gaps in knowledge. Further, structure and critical insight into the meaning of current findings could be improved. I have few comments that should help the authors to improve the quality and relevance of this review.

1. Although it’s not a systematic review I would mention somewhere how the literature was searched, how cited sources were selected, whether the authors searched specific journals, and specify if they limited their results to a specific date range. Alternatively, this should be addressed in the conclusive part of this review as potential limitations if the sources are not the most up-to-date or biased.
2. Each section summarizes information but does not point out weakness or strengths of selected papers, and does not identify gaps in the literature. Overall, better critical evaluation of the literature is needed. This will allow both the authors and readers to come up with new questions about the problem and/or answer the research question this manuscript is based on.
3. I think that the authors’ research question is too broad. The authors address a range of important aspects associated with functional outcome. Although this is good as it provides general information on the topic, the amount of information provided in this manuscript may be both overwhelming and confusing, especially to the reader unfamiliar with the literature. I would recommend that the authors narrow down their focus (shorten the review, choose the most important topic) and/or better outline the structure of their manuscript in the beginning of their manuscript.
4. I noticed that the authors address the concept of “cold cognition” but do not discuss “hot cognition”. Was this intentional? Would they like to address this somewhere in the manuscript? Hot cognition is likely to play an important role in global functioning and should be mentioned.

Minor details

-add references to statements included in 2.4. Or mention if the literature is limited.

-Please consider modifying Figure 1. The purpose of this figure is unclear as it does not offer clarification or additional information.

-Title: I would consider choosing a shorter title that reflects more accurately reflecting the content of this manuscript. Please consider removing “difficult lives” and rather focus on concepts such as “functional outcomes” and “review of the literature”.