**Ref: JAD\_2016\_486**

**Title: Discrete neurocognitive subgroups in fully or partially remitted bipolar disorder**

**Journal: Journal of Affective Disorders**

Background: Neurocognitive impairment in remitted patients with bipolar disorder contributes to functional disabilities. However, the pattern and impact of these deficits are unclear. Methods: We pooled data from 193 fully or partially remitted patients with bipolar disorder and 110 healthy controls. Hierarchical cluster analysis was conducted to determine whether there are discrete neurocognitive subgroups in bipolar disorder. The pattern of the cognitive deficits and the characteristics of patients in these neurocognitive subgroups were examined with analyses of covariance and least significance difference pairwise comparison. Results: Three discrete neurocognitive subgroups were detected: one that was cognitively intact (46.1%), one that was selectively impaired with deficits only in processing speed (32.6%), and one that was globally impaired across verbal learning, working memory, and executive skills (21.2%). The globally and selectively impaired subgroups were characterized by greater perceived stress and cognitive complaints, poorer work capacity and reduced quality of life compared to patients who were cognitively intact. Limitations: The study design was cross-sectional which limits inferences regarding the causality of the findings. Conclusion: Globally and selectively impaired bipolar disorder patients displayed more functional disabilities than those who were cognitively intact. The present findings highlight a clinical need to systematically screen for cognitive dysfunction in remitted bipolar disorder and to target residual cognitive dysfunction in future treatment strategies.

Comment: Based on recent findings by Burdick et al.’s the authors aim to test whether there are discrete neurocognitive subgroups among BD patients. Furthermore, they want to assess to which extent neurocognition affects functional abilities, perceived stress, subjective cognitive complaints, work capacity and QoL. Pooled data from 4 studies was examined using discriminant analyses, multiple regressions and ANOVAs. Three neurocognitive groups were detected: a cognitively intact, selectively, and globally impaired. The cognitively impaired groups displayed greater stress, cognitive complaints, poorer work capacity, and reduced QoL. I commend the authors for 1. Gathering a large BD sample, 2. Using a range of statistical techniques to thoroughly assess the data, 3. Examining the link between cognition and global functioning. Given these strengths this paper presents novel findings that deserve to be published in this journal. I would, however, like to recommend a few revisions to improve the understanding of the study rationale, methodology, and interpretation of the findings.

Title: I would mention the words “global functioning” or refer to functional abilities.

Introduction: I would encourage the authors to provide additional information on the link between cognition and global functioning, e.g. perceived stress, QoL. I would also add some mention of potential cognitive differences or similarities between fully remitted/partially remitted BD patients. This would “solidify” the study rationale, and help the readers understand 1.why it is important to study such topic and 2. why studying remitted/partially remitted BD patients is meaningful.

Methods: please explain why exclusion criteria for HC included dyslexia and not intellectual disability, or learning disabilities for instance? Why does this exclusion criteria apply to HC only?

-did the authors plan to correct results for mood symptoms? Although there are no statistically significant differences across groups subthreshold mood symptoms have been shown to modulate cognition. This issue should be addressed appropriately.

-what kind of diagnostic tool did the 4 studies included in this manuscript use to determine the participants’ BD diagnosis? E.g.SCID? How many participants were euthymic/depressed/etc.?

-could the authors provide the type of comorbidities in each “cognitive subgroup”?

-how did the authors select the questionnaires assessing work capacity, subjective cognitive difficulties etc.?

-why didn’t the authors select immediate learning for instance, rather than creating a composite score including both immediate learning and recall? The former measure may be even more diagnostically relevant than the latter.

-why didn’t the authors select a work and social adjustment scale that could be applicable to both BD and HC? If they couldn’t standardize WSAS to HC, would it make sense to use this measure anyway?

-did the authors check the data for collinearity? Could they provide the correlational matrix between cognitive and functional scores?

-could the authors please describe in their statistical analyses section the approach used for the multiple regressions (mentioned in 3.3)? The number of variables included in these regressions is certainly elevated. Could this be a source of concern when interpreting the findings?

-why was benzodiazepine considered as an individual variable instead of being included in “medication”?

Results: in 3.3 could the authors clarify what they mean by “cognitively impaired subgroup”? Are they referring to globally or selectively cognitively impaired participants?

Discussion: could the authors please clarify if on page 11, line 6 and on page 12, line 2, they meant “age” or “age of onset”? I thought they were indeed age differences across BD groups.

Details: In 1.1. please discard 1) and 2) as it is more confusing than helpful.