Ref: JAD\_2016\_164

Title: Possible influences of cognitive impairment on activities of daily living in patients with bipolar disorder

Journal of Affective Disorders

**Background:** Many patients with bipolar disorder (BD) experience debilitating cognitive deficits, with risk of impaired occupational and psychosocial functioning. However, knowledge on how these deficits impact the patients’ ability to perform Activities of Daily Living (ADL) is sparse. Aim: To explore the relation between impaired cognitive function and the ability to perform ADL in patients with BD. Methods: A total of 42 patients with BD, in remission (Hamilton Depression Rating Scale and the Young Mania Rating Scale ≤ 7) and subjective cognitive complaints (≥ 13 on the Cognitive Complaints in Bipolar Disorder Rating Assessment questionnaire) were included. Objective neurocognitive function was evaluated with a short comprehensive cognitive test battery and ADL ability was evaluated with the observer- and performance-based Assessment of Motor and Process Skills (AMPS). Results: Deficits in processing speed, but not in memory or executive function, correlated significantly with ADL process impairment (r=0.37, p=0.02). Dividing the sample into a functionally abled and a disabled group according to their ADL ability showed that reduced processing speed was associated with decreased ADL ability also after adjusting for the effect of age, gender, and subclinical depressive symptoms (p=0.03, Wald=4.69, exp(B)=1.45, (C.I.: 1.04-2.03)). Limitations: The generalizability of the study is limited by a small sample size and a large proportion of the patients were women. The patients were included based on subjective cognitive complaints. Conclusions: Reduced processing speed indicated decreased ADL ability in patients with BD. A performance-based evaluation to assess cognition and ADL ability in clinical setting could prove useful to disentangle and tailor the treatment of patients with BD and functional impairment.

**Comment:** Individuals with BD are exposed to a number of challenges including mood fluctuations, cognitive deficits, fewer personal resources, lower work productivity, and personal limitations. I therefore commend the authors for addressing this intriguing topic and think that this study has an extremely relevant public health goal, as it encourages the identification of effectively tailored treatment interventions and maximizes cost containment. I am glad the authors included both self-rated, observed and performance based measures as the impact of mood, self-confidence and motivation play a role in both cognition and global functioning. As I read the manuscript I found some areas in which I would have appreciated greater clarity. In particular, I believe the paper could be further strengthened by addressing the following points.

Title: The authors may consider changing the title to refer to processing speed (rather than cognitive functioning) and discard “possible”

Abstract

1. A clearer definition of how the authors define ADL both in the abstract and manuscript seems necessary. For instance in the abstract the authors mention impaired occupational and psychosocial functioning. Is ADL meant to be home-related activities?
2. Please provide N of females/males, mean age and medication status. No need to provide statistical data in the abstract.
3. The authors could provide additional information regarding “functionally abled/disabled” (e.g. based on AMPS cut-off scores). I would also encourage the authors to use less stigmatizing expressions such as less functional rather than “disabled”.
4. Please reformulate/edit the sentence “generalizability of the study is limited by…a large proportion of the patients were women”. I guess what the authors may mean, but I would recommend a more diplomatic expression to say this such as “gender ratio imbalance”.
5. Conclusions: the authors may need to edit/reformulate what “disentangle” refers to. Also the authors could consider mentioning how AMPS may be relevant in BD, and whether observed, self-rated or performance based measures of cognitive functioning are best predictors of AMPS.

Highlights

1. Please check for character count (max 85). I would be precise when talking about processing speed vs mentioning cognitive impairment as the two words refer to different concepts.

Introduction

1. The authors are correct in saying that ADL is an underexplored research field in BD. There is however an increasing body of research looking at this topic (Moore et al. 2010) looking for instance at the usefulness of ecological tests and tasks simulating real world tasks. Please cite or discuss Laloyaux et al. 2013 (shopping task predicting global functioning in BD), Pattanyak et al. 2012, Martinez-Aran et a. 2007, Althuler et al. 2008, Bowie et al. 2010, Laroi et al.’s work.
2. The authors could broaden their introduction and make the rationale of their study a bit more robust by discussing 1. The link between self-rated cognitive skills, ADL and cognitive abilities. Why is it important or why do they want to explore this? 2. What kind of ADL are usually impaired in mood disorders if any? Are there differences in ADL difficulties when compared to individuals with cognitive deficits but good physical health, e g. dementia.
3. Since some authors found a correlation between cognitive deficits and duration of illness/number of hospitalization, e.g. Cao et al. 2016, how do the authors think this would affect cognitive functioning?
4. Previous studies define ALD as communication, financial limitations, residential independence and poor social skills. Which domains are the authors interested in and why?
5. From reading the literature I gather that while the link between reduced cognitive functioning and reduced ADL is well-established there is little out there in terms of the predictive value of cognitive tasks on global functioning. I wonder why the authors approached this topic in such an exploratory way and did not make more direct hypotheses.

Methods

1. Could the authors clarify why they selected such a broad age range for recruitment purposes
2. I noticed that there are no BD-NOS in the sample. Is this intentional?
3. Why didn’t the authors include a control group?
4. It is also unclear why the authors excluded ECT only if it occurred in the previous 3 months.
5. How did they define current substance use?
6. How do they define physical illness or “handicaps”. I am particularly curious to know if they excluded cardiovascular, neurological, endocrine and metabolic diseases. Also the word “handicap” may be misinterpreted. What do they refer to?
7. Why did they include patients taking benzodiazepines since it may slow patients down/sedate them and impair their cognitive functioning.
8. AMPS: the authors should consider clarifying that this scale includes both motor and planned tasks and how they usually correlate with neuropsychological and self-rated tasks. Also can the authors please provide previous findings related to AMPS in psychiatry. Were the assessments of ADL influenced by time in any way? E.g. was the quality of actions dependent of how quickly they were performed. Further, if I understand correctly, the rater selected two tasks found to be meaningful and relevant for the participants. I wonder if this process of selection was easy, whether tasks were influenced by gender, whether there were easier and more difficult tasks, and if so, how to compare performance on these two tasks. Overall how is the interrater reliability for AMPS measures and are they stable over time?
9. Could the authors provide additional information on the analyses shown in Table 4. The regression does not appear to be discussed in the methods section. Also despite the small sample size and high number of potential variables that may predict ADL I wonder whether the authors consider conducting hierarchical analyses, e.g. entering first a block of demo variables, then mood, then self-rated cognitive performance, to find predictors of AMPS scores ?
10. The SCIP assessment of cognitive abilities appears to be time-based. Is this correct? If so, how could this be confounding effect for the interpretation of the current results?

Results, discussion & Conclusions

1. How do the authors explain that high HDRS correlated negatively with processing speed?
2. In the manuscript please clarify the fact that COBRA scores were negatively correlated with SCIP verbal learning. Also I couldn’t find the table with this specific finding.
3. What is the cut-off score separating “functionally able” to “functionally less able” individuals?
4. I noticed that the authors refer to findings in older results and wonder if comparing the current findings to Gildengers is relevant? Didn’t age affect these findings?
5. I would appreciate it if the authors discussed the effect of medication and type of tasks in the interpretation of processing speed in BD.
6. The authors should be more thorough when explaining the reason that having a majority of women has an impact on their findings. More biological background is required.
7. I am surprised that the authors did not highlight their ROC findings as they have significant relevance in terms of diagnostic predictability.
8. Also could the authors discuss the impact of assessing ADL based on tasks the participants is familiar with vs a new task. Could this be a confounding factor?