**Manuscript:** Type 2 diabetes mellitus a potentially modifiable risk factor for neurochemical brain changes in bipolar disorders

**Outcome:** accepted pending minor revisions

**Comment:** Hajek et al.’s study aims to determine whether type2 diabetes mellitus is a risk factor for neurochemical alterations in bipolar disorder. The authors employed magnetic resonance spectroscopy to measure changes in NAA and Cr levels in the prefrontal regions. The authors found that these metabolites were depleted in patients with bipolar disorder and diabetes mellitus and they were elevated in controls and euglycaemic patients. These remarkable findings could help develop clinically useful behavioral interventions to prevent and treat bipolar disorder.

*Strengths:* originality of the work, strong rationale and well-designed experiment, conclusions are well-formulated and are consistent with the findings of the study.

*Revisions:*

Page 8: could the authors explain why they selected the left prefrontal cortex as the primary region of interest? The authors explained the localization of this region by referring to previous MRS trials in relatives of bipolar subjects and lithium effects on NAA. However, a stronger rationale in keeping with the aims of the current study may be needed.

Page 9: did the authors consider comparing BD with IR/GI to controls with IR/GI? I assume that the sample size would have been an issue however what would the authors have expected from this comparison? Should this be addressed in future studies? It would be perhaps worth addressing this topic in the conclusions.

Page 9: could the authors reformulate how they investigated if NAA and Cr levels were associated with impaired energy metabolism. Did they conduct a regression analysis for NAA and an ANOVA for Cr? If so why?

What is the statistical significance threshold for the analyses of this study? What kind of multiple comparison correction was applied?

Statistical results should be presented in the APA style if possible. Effect size and coefficient of determination should also be mentioned for correlational analyses.