**Association of thalamic hyperactivity with treatment resistant depression and poor response in early treatment for major depression. A resting state fMRI study.**

*Yamamura et al.*

**Comment: Minor revisions required**

By applying fractional ALFF the authors aimed to identify potential alterations in spontaneous neuronal activity associated with TRD. The authors also performed correlational analyses between HRSD scores and fALFF values in brain regions with differing activity for patients with and without TRD. The results suggest that increased right thalamic fALFF values are characteristic of TRD patients. The percent change in the HRSD was negatively correlated with fALFF values in non-TRD patients. TRD patients also show increased fALFF values in the IFG, IPL, and vermis compared to non-TRD and HC.

I am overall satisfied with the way the authors addressed my comments. I would like to recommend few minor revisions that would improve the quality of this manuscript further.

1. The acronym fALFF in the title should be preceded by the full word. Alternatively the title could be reformulated to include “Amplitude of Low Frequency Fluctuations”.
2. Page 3: please reformulate sentences 13to 15, possibly referring to “biological mechanisms” underlying TRD”. Also fMRI can measure both task-independent and task specific neural function. It is important to clarify this.
3. Page 4, line 6. I would say “associated with cognitive abilities and mood reactivity”. The two concepts are not synonyms.
4. Page 21, line 5 to 9. I am glad the authors took onboard my suggestion to talk about the clinical relevance of these findings. I think they should reformulate this sentence (shorten it and split into two statements) to clarify what they mean by individualized treatments. For instance at line 7 they could start a new sentence stating “these techniques could be used as complementary assessments methods”. Further, instead of using “the method” please state the actual name of the method (I assume they are referring to using resting state fMRI along with f/ALFF measures).
5. Page 20, line 9. Please add a few more details related to the study with ref.82. Right now the sentence is a bit ambiguous and incomplete (“this result supports a previous study).
6. Page 13, line 6 please correct “patients” instead of “patents”
7. Page 14, lines 17 to 19. The sentence is unclear. Please reformulate, for instance by starting the sentence with “In patients with non-TRD only the right….” and finishing with “after removing the effect of the duration of the current episode”
8. Page 16, line 6. Please complete this sentence by saying “the first to demonstrate this relationship directly using…..”. (add the name of the methods used in this paper, it will make this statement more compelling).