**Manuscript:** Fronto-parietal activation during response inhibition predicts remission to antidepressants in patients with major depression: outcomes from iSPOT-D

**Overall comment:** the authors explore the relationship between neural activity, remission and medication type in major depression using a functional MRI investigation. Rationale, concept and design are novel, of very high quality and deserve to be published in this journal. I think that the discussion could be improved by addressing the clinical implications and/or possible mechanisms underlying the current findings.

**Introduction:**

1. Did the authors have specific hypotheses associated with the selection of the treatments (besides being commonly administered in MDD patients)?
2. Did the authors expect variations in results between the 2 SSRI treatments? Did they expect differences due to the impact of these medications on neurotransmitters or other biological mechanisms? It may be worth discussing these research questions in the introduction and conclusion.
3. Did the authors have hypotheses associated with the level of treatment response (among participants who did not exhibit full remission) and neural activity?

**Methods**

1. Were participants non-medicated only in terms of anti-depressants or overall for all kind of neuropsychiatric diseases?
2. Could the authors mention whether the participants suffer from comorbid disorders such as substance abuse etc.
3. Overall how was compliance measured?
4. 8 weeks is a relatively short period to measure treatment response for anti-depressants. Could the authors comment on this?
5. Given the severity of the symptoms (see Table 1) could the authors comment on why some participants were unmedicated and how was their overall global functioning? Please mention N of unmedicated patients.
6. Did the patients included in this study ever take part in behavioral interventions?

**Conclusions**

1. Do the authors imply that treatment response to anti-depressants may be mediated by cognitive mechanisms?
2. If so could they please provide references and/or potentials explanations on which biological mechanisms may be involved?
3. Page 17: changes in neural efficiency may be viewed in terms of changes in functional activation in absence of changes of cognitive performance. The authors could discuss this topic a bit further and add references to this interesting topic.
4. How do the authors interpret the absence of results associated with the other fMRI tasks. Is this related to the different level of difficulty across tasks? Or rather due to the type of cognitive abilities measured by the Go/No-Go task?
5. How do SSRI/SNRI treatments affect fMRI activity? How do they affect executive functions? The authors could integrate previous findings to provide a more thorough interpretation of their results.

**Technical comments**

1. Abstract: last sentence of the results section could be improved. The authors could mention whether the SNRI remitters and/or non-remitters showed the opposite pattern of results.
2. Page 5: Pre-potent refers to “prepotent”?
3. Please mention the achronym DLPFC at page 13 as it is the first time where “dorsolateral prefrontal” appears.
4. Supplemental figure 1: please edit/proofread content in the flowchart and caption
5. Table 1: please mention that duration is measured in years (or months?)