

MANUSCRIPT NO.2 (27893) ANSWERING REVIEWERS

Reviewer #1:

- a) Excellent paper. Well written with important findings.**

Our Response: We thank the reviewer for a positive evaluation of our work.

Reviewer #2:

- a) This manuscript presents data on a structural MRI study using voxel-based morphometry in a sample of 20 patients with schizophrenia and preserved insight, 20 clinically and demographically-matched patients except for poor insight and 20 healthy participants. The authors found lower grey matter volumes in a lot of brain areas in patients with poor insight. From these findings, they suggest that clinical insight is dependent on complex neurocognitive interplay with contributions from multiple neural networks. The study is well designed and the manuscript is clearly written and easy to read all throughout.**

Our Response: We thank the reviewer for his/her encouraging comments.

- b) My main concerns are a) the lack of originality which may decrease its interest for potential readers, and b) the potential effect of confounding factors. Although the authors have done an effort for controlling several clinical factors, some others such as medication effects could still be playing a role. Stable medication and chlorpromazine equivalents may not be enough to control for such effects and authors should clarify whether there were differences in the type of antipsychotic medication between both groups.**

Our Response: As suggested by the reviewer, we have now detailed the antipsychotic medications prescribed to all patients of both the preserved and poor insight groups (please see revised Table 1).

- c) Second-generation antipsychotics are associated with larger grey matter volumes than first-generation ones. Differences among the presence and quantity of particular compounds belonging to these two families could influence their results.**

Our Response: We thank the reviewer for raising this important issue. In addition to describing the exact antipsychotic medications for both patient groups (please see revised Table 1), we have discussed this factor as a possible limitation of our study (please see Discussion, last paragraph).

Reviewer #3:

- a) The purpose of this study, using a categorical approach, maintained clinical insight as well as those with healthy participants was relatively poor clinical view clearly in stable patients with schizophrenia in terms of regional gray matter to detect abnormalities. Forty stable schizophrenia outpatients (20 with preserved and 20 with poor insight) and 20 healthy participants were included to study. The Birchwood Insight Scale (BIS; self-report measure) was used for insight. Authors found that the lower fronto-temporal,**

parahippocampal, occipital and cerebellar grey matter volumes in patients with poor insight, compared with preserved insight patients and healthy participants. Preserved insight patients did not differ significantly from healthy participants. When scanned previously literature, Magnetic resonance imaging (MRI) studies revealed fronto-temporal cortical gray matter volume reductions in schizophrenia. However, it can be determined that there is not much literature. The authors have made comparisons through the concept of insight.

Therefore study is valuable. I think the study will provide an important contribution to the literature. The number of patients and control subjects included in the study is enough. Introduction and discussion section are sufficient. Adequate and appropriate literatures were used in the study.

Our Response: We are grateful to the reviewer for his/her encouraging comments.

- b) However, The weakest point of the work for me; " Healthy participants had more years in education than poor insight patients [$t(38)=2.11$, $P=0.04$] but differed only at a trend level when compared with preserved insight patients [$t(38)=1.77$, $P=0.08$]. Healthy participants also had higher NART IQ than poor insight patients [$t(38)=2.47$, $P=0.02$] but did not differ from preserved insight patients". Which is part of the results. I think that the results of these parameters that affects clinical important. Nevertheless, I suggest accept this manuscript.

Our Response: We accept this criticism. We have added new text (please see Discussion, first paragraph) discussing that although lower IQ in patients with schizophrenia, relative to the healthy population, is a common finding, this may be particularly true for those with poor insight and also explain our finding of significantly fewer years in education in the poor (but not preserved) insight patient group, compared with the healthy participant group.