Reviewer's report

Title: Differences in working memory load produce an abnormal pattern of P300 amplitude in schizophrenia

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Reviewer: Margaret Niznikiewicz

Reviewer's report:

“The differences in working memory load produce an abnormal pattern of P300 amplitude in schizophrenia,” is potentially an interesting study on the electrophysiological correlates of cognitive dysfunction in schizophrenia. The authors used a working memory paradigm (n-back) within the context of the P300 study to probe WM dysfunction in schizophrenia.

However, there are several problems with the study that make it difficult to assess exactly what contribution this study makes to the field of clinical neuroscience.

I completely do not understand what the authors are trying to say with the sentence describing ‘exclusion criteria’: page 5: “Exclusion criteria for this study were any current or past psychiatric diagnosis (excluding schizophrenia in the schizophrenia patients)” – I am sure the authors did not try to exclude schizophrenia diagnosis in schizophrenia patients – please clarify.

This is really odd to perform a clinical evaluation 1 month after the subject was included in the study – please clarify.

One of the major issues with the study is the description of the task. The authors need to provide a more detailed description so that one could make a judgment about exactly what cognitive processes took place during the task. As it stands right now, we are not told how the two equal numbers – I assume identical digits - were displayed. Were they displayed simultaneously, or in a sequence. If in sequence, what was the ISI. The authors need to give the ISI for all their conditions as this variable influences the task in a crucial way.

The subjects made a response – was the use of right and left hands counterbalanced across subjects?

The decision to create epochs with 500 msec baseline is rather strange – the typical baseline is 100-200 msec unless there is a methodological/theoretical good reason to extend it – what was the authors’ reasoning? In addition, this baseline in especially problematic given that we are not told what the ISI is and how it relates to the length of the baseline.

Please report unadjusted DF only.

The use of ‘virtual electrodes’ is strongly discouraged. With 80 electrodes it is perfectly legitimate to select a subset of electrodes that represent maximal voltage/group separation for a given paradigm and use these electrodes in the
stats analyses. Otherwise, one can use a grouping factor of ROI or region and use actual electrode values within each region. The use of virtual electrodes largely obscures the real voltages on the scalp and often creates a false impression of what is going on in the data. Thus, for this paradigm, it is hard to say exactly what effects the authors obtained.

In addition, the way to go about the stats analysis is to start from an omnibus M/ANOVA with 1 between factor of group (SZ, NC) and two within factors of condition (3 levels: 0, 1, 2 n-back) and region/electrode (number of levels dependent on approach/electrodes chosen) and proceed from there. The main effects and interactions should dictate follow up analyses.

I would also like to see group comparison for the 0 back – in spite of this paradigm presenting WM demands, it is a visual P300 paradigm and reports often do not find a reduced visual P300 in schizophrenia.

Finally, while reporting stats results, it is OK to say that there is a trend level difference in amplitude/latency but it is not OK to say that, e.g., latency was more prolonged in patients but the difference was not significant – the result is that there was no difference in latency – or it was prolonged at trend level.

In the Discussion, the authors make a claim that different WM demands produced abnormal patterns of P300 amplitude in schizophrenia. This is exactly what not happened. In fact, this is what is noteworthy in the study: patients did not modulate P300 as a function of a WM load.

Kok (2001) is cited in the context of a notion of a ‘phonological loop’ taking away from resources devoted to the generation of the P300. Kok never mentioned this concept: please read his review carefully.

The authors discuss ‘a trend’ in the group differences in the high memory condition. However, no trend is reported in the stats section. One can discuss a trend if one reports it – otherwise – there is no trend to discuss.

I do not understand what the authors are trying to say when they discuss a WM update process which ‘fails to be fully executed’ in normal controls at high WM load – please clarify.

In conclusion, I am not convinced at all by the explanation offered by the authors regarding the lack of P300 modulation in a WM task in a patient group.

Minor Problems:
Please, edit the paper in terms of English grammar and word use.
People typically talk about P300 component not wave or waveform which is used to describe the entire epoch.
What do the authors mean by ‘altered WM processing’ – page 3 – please explain the concept better.
Please report your results in past tense.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.