Reviewer’s report

Title: Cognitive correlates of repetitive transcranial magnetic stimulation (rTMS) in treatment-resistant depression- a pilot study

Version: 1 Date: 19 June 2012

Reviewer: Dave Hayes

Reviewer’s report:

In the article titled “Cognitive correlates of repetitive transcranial magnetic stimulation (rTMS) in treatment-resistant depression- a pilot study” the authors aimed to investigate the potential impact of rTMS of the left DLPFC over 20 days on cognitive functioning, as measured using a task (mCST) and a neuropsychological test battery (RBANS).

This pilot work revealed interesting and potentially clinically relevant results, showing improvements in cognitive measures beyond what would be expected by repeated performance. Moreover, the manuscript is clear and concise.

Before publication, however, I believe the following minor essential revisions should be considered:

Abstract:
The inclusion of the 8 healthy volunteers and the general comparison should be included in the abstract.

The use and findings regarding the depression scores (BDI, HAMD) should be noted here.

Background:
1 Hz< should be >1 Hz for consistency

How were the 8 of 54 participants chosen? It is not clear if they performed the task again (i.e. within the same timeframe as the depressed subjects) or whether their prior initial data was used. Given the latter case, are the results replicable using another random sample from the group of 54?

Results:
It is noted on pg. 8 that “In case any participants missed experimental days…” It should be noted how many subjects missed treatments and on which days.

It is not clear that the use of Sidak’s correction is appropriate given that it requires the assumption of independent sampling – unlike the Bonferroni correction. Why have the author’s not chosen to use the Newman-Keuls post hoc test?
The comparison statement beginning on pg. 10 that states “only patients performed significantly more accurately....” is somewhat incorrect, given that (it appears) that the analyses for patients and volunteers was done separately. If compared directly, given the data, it looks as though the variability in each group would make it statistically insignificant from the other. In other words, though only one group has reached significance for accuracy, it is not appropriate to claim/imply that the two groups are significantly different without performing the necessary between-groups test.

Discussion:
The comment that “it’s unlikely that the improvement...was due to practice...not observed in healthy volunteers” seems somewhat strong given the small sample size and what appears to be greater variability in accuracy for the volunteers in the before/block 1 condition compared to patients, as well as the appearance of better performance in general during this period for patients > volunteers. At this sample size, a single subject with highly variable performance can greatly affect the overall statistical significance. These and related issues should be raised in the limitations section. Overall, because this is pilot work in a small sample, the authors should always be careful not to overstate the importance of their findings.

Pg. 13 one too many “right's” for right DLPFC.

Another possible control would be having the volunteers receive the rTMS treatment. Along these lines, the authors might consider recent work by Schaller et al., 2011 looking at changes in mood following rTMS of the IDLPFC. Is it possible that improved mood in both groups (healthy and patient) would lead to improved accuracy?

Also, (although a minor point), I wonder if, because subjects perform so well across both blocks, the authors might anticipate that a ceiling effect might prevent the detection of real differences in these groups.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests