Reviewers report

Title: Risk assessment and reward processing in problem gambling investigated by event-related potentials and fMRI-constrained source analysis

Version: Date: 15 June 2014

Reviewer: Raffaele Cacciaglia

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The manuscript “Risk assessment and reward processing in problem gambling investigated by event-related potentials and fMRI-constrained source analysis” by Stephan F. Miedl, Thorsten Fehr, Manfred Herrmann, Gerhard Meyer investigates risk assessment and reward processing in problem gamblers (PG) vs. occasional gamblers (OG) using fMRI-constrained source modeling event-related potentials (ERPs). The authors implemented a quasi-realistic blackjack game where participants were asked to take a risky decision (drawing or not a card), and analyzed EEG event-related responses during two distinct phases of the game: a former phase accounting for the evaluation of risk and a latter phase as an index of reward processing. The authors report significantly larger source moments in PG vs. OG for high-risk vs. low-risk decisions during the risk assessment phase. This is revealed by the increased ERPs amplitude in the time window between 600-800 ms, driven by the thalamus, orbitofrontal and superior frontal regions. Additionally the authors report enhanced amplitudes during reward processing in PG vs. OG, in two different time windows (100-150 ms and 390-440 ms) driven by rostral cingulate and superior-frontal/premotor regions, respectively. They conclude that pathological gambling is associated with stronger cue-related craving during risk assessment and with modulation of early affective reward-related components. Based on fMRI constrained source analysis data showing different regions involved in distinct temporal windows, the authors also conclude that in the PG group risk assessment appears to evolve in a top-down fashion, while reward sensitivity is likely based on bottom-up processing.

The background of this study is well explained, and the employed methodology is sound. Of particular relevance, is the employment of previously reported fMRI networks to constrain source localization of EEG data.

This work is of interest and it represents a significant advance in understanding the neural bases of pathological gambling.

There are, however, few points that need to be addressed:

A) Major compulsory revisions

RESULTS

1. Page 14, lines 13-14. The authors report a significant three-way interaction
(LAT*RISK*GROUP) indicating a p-value of 0.052, which is in fact not significant. The authors should report this result as a trend to significance.

B) Minor essential revisions

RESULTS:

1. Page 14, lines 20-22. The authors report a significant group effect in the post-hoc t-test at electrodes Fz, Cz, and Pz, but they do not explain the direction of such differences. Although this is later explained in the caption of Figure 2 (page 26), this information should also be reported in the text, as already done for the results above. The sentence “Post-hoc tests indicated at midline electrodes Fz (t[1,22]=2.25, p=0.035), Cz (t[1,22]=2.26, p=0.034), and Pz (t[1,22]=3.33, p=0.038; see Figure 2, upper part)” is therefore incomplete.

2. Page 15, line 25, and page 16, lines 1-2. The reported results are inconsistent with the caption of Figure 3 and also with the abstract. More specifically, the authors report that “PG showed larger source moments than OG between 100 and 150ms in the left anterior cingulate gyrus followed by a trend to enhanced source activity in PG in right superior frontal gyrus between 390-440ms”. However, these results appear to be swapped in the caption of Figure 3 (page 26, lines 19-21), where the authors actually report a statistical trend for the 100-150ms time window (p = 0.067), while reporting a significant result for the 390-440ms time-window (p<0.05). This issue needs to be clarified.

3. Page 16, line 2. The authors report a trend to enhanced source activity in PG vs. OG in the right superior frontal gyrus between 390-440 ms during reward processing. However, in Fig. 3 (lower part), the black box indicating the statistical trend is located in a region labeled “middle frontal gyrus”. Can the authors clarify whether the effect was found in the superior or rather in the middle frontal gyrus?

DISCUSSION

4. Page 18, lines 10-12. The authors report “A trend to higher mean amplitude between 100 and 150ms in PG compared to OG in the win vs. lose difference wave at fronto-central electrode positions (F3, Fz, Cz) resulted from higher amplitude in the win relative to the lose condition exclusively in PG”. However, in the Results section, they report an inverse pattern. At page 15, lines 4-6, it is in fact reported “Post-hoc tests indicated significantly lower mean amplitude values (difference: win vs. lose) in PG compared to OG at electrode positions F3 (t[1,22]=2.27, p=0.033), Fz (t[1,22]=2.91, p=0.008), and Cz (t[1,22]=2.27, p=0.034; see Figure 2, lower part)”. This issue should be clarified.

C) Discretionary revisions

ABSTRACT

1. The “background” subsection of the abstract actually contains a description of the methodology. This section should instead contain a brief summary of previous findings on the topic, and a brief statement supporting the research
questions.

2. In the “results” subsection of the abstract, the authors mention that no significant differences were found for behavioral data. However, there is no description of behavioral assessment in the previous “methods” subsection. I encourage the authors to explicitly state “Both groups did not differ in reaction times”, which may be clearer for the reader.

3. Again, in the “results” subsection, the authors report “differences” between the PG and OG group in the later time window (390-440 ms) of reward processing (page 2, line 17). I encourage the authors to be more specific and to mention the direction of such differences (i.e. increased source moments in PG v. OG).

BACKGROUND:

4. Page 3, line 2. Please enter the reference for the DSM V.

5. Page 3, line 5. “Pathological gambling shares core features of substance addictions” should be “Pathological gambling shares core features with substance addictions”

6. Page 3, lines 6-7. “As context specific environment seem to play…” should be “As context specific environment seems to play…”

7. Page 3, line 14. “…and enhanced fromo-parietal activation…” should be “…and enhanced fronto-parietal activation…”

8. Page 3, line 18. Please explain the abbreviation “ERN”, I presume this is error-related negativity.

9. Page 3, line 24. Please explain the abbreviation “ACC”, I presume this is anterior cingulate cortex.

METHODS

10. Page 5, lines 16-17. Could the authors specify which structured clinical interview they used?

11. Page 9, line 12. Please explain the abbreviation “GFP”, I presume this is global field power.

12. Page 9, line 26. “…were corrected for sphericity where necessary” should be “…were corrected for sphericity violation where necessary”.

RESULTS


14. Page 14, lines 13-14. “…were statistical significant…” should be “…were statistically significant…”

DISCUSSION

15. Page 16, line 17. “There were trend to…” should be “There were trends to…”
Report signed by:
Raffaele Cacciaglia, PhD.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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