21730-Answering to editor and reviewers

ESPS Manuscript NO: 21730

Title: Functional Magnetic Resonance Imaging of Internet Addiction in young adults

Authors: We would like to thank the Editor and Referees for giving us the opportunity to further improve our manuscript through their comments. We dealt in details with all the requests.

The changes in the manuscript are yellow-highlighted.

EDITOR'S COMMENTS

Comment #1 and #2

In title page: Please offer the postcode of institutions.

Authors' response: done

Comment #3

Any manuscript describing a study (basic research and clinical research) that used biostatistics must include a statement in the Materials and Methods section affirming that the statistical review of the study was performed by a biomedical statistician. Statistical review is performed before the submission or after peer-review. The author invites an expert in Biomedical Statistics to evaluate the statistical method(s) used in the study, including but not limited to the *t*-test (group or paired comparisons), chi-square test, ridit, probit, logit and regression (linear, curvilinear, or stepwise) modeling, correlation, analysis of variance, and analysis of covariance. The review by the biomedical statistician is conducted with respect to the following points: (1) Statistical methods are adequately and appropriately described when they are used to verify the results; (2) Whether the statistical techniques are suitable or correct; (3) Only homogeneous data can be averaged. Standard deviations are preferred to standard errors. The number of observations and subjects (*n*) is given. Losses in observations, such as drop-outs from the study, are reported; (4) Values, such as ED50, LD50 and IC50, have the 95% confidence limits calculated and have been compared by weighted probit modeling (using the functions

described by Bliss and Finney); and (5) The word "significantly" is replaced by its synonyms (if it indicates extent) or the *P* value (if it indicates statistical significance). In addition, a copy of any approval document(s)/letter(s) or waiver should be provided to the BPG in PDF format.

Authors' response: All statistics were performed by Dr. Gianna Sepede (and the statement has been added to the title page).

As requested, we also added the following paragraph in the "Materials and Methods" section: "Statistics were performed by Dr. Gianna Sepede, who has a certificated experience in Biomedical Statistics, Systematic Reviews and Meta-analysis. In the present paper, PRISMA 2009 checklist (http://www.prisma-statement.org/) was used to describe eligibility criteria, conduct the search, select the studies and report the qualitative synthesis results. Statistical methods were therefore (1) adequately described, (2) correct and (3) conducted on homogeneous data. Number of subjects and dropouts were given. When appropriate, confidence limits (4) and significant p values (5) were calculated and reported.

We have no additional paper/letter/waver to provide.

A biostatistic statement copy was also provided in PDF format.

Comment #4

A conflict-of-interest statement is required for all article and study types. In the interests of transparency and helping reviewers to assess any potential bias in a study's design, interpretation of it results or presentation of its scientific/medical content, the BPG requires all authors of each paper to declare any conflicting interests (including but not limited to commercial, personal, political, intellectual, or religious interests) in the title page that are related to the work submitted for consideration of publication. In addition, reviewers are required to indicate any potential conflicting interests they might have related to any particular paper they are asked to review, and a copy of signed statement should be provided to the BPG in PDF format.

Authors' response: All Authors do not report any conflict of interest. The conflict-of-interest statement was reported in the manuscript, and a signed copy was provided in PDF format

Comment #5

Basic research and clinical research studies require a data sharing statement. The data sharing statement will be provided in the title page, and will be presented in the following form: Technical appendix, statistical code, and dataset available from the corresponding author at Dryad repository, who will provide a permanent, citable and open-access home for the dataset. In addition, a copy of the signed statement should be provided to the BPG in PDF format.

Authors' response: No additional data are available. Following the wording sample suggested in the "Guidelines and Requirements for Manuscript Revision-Systematic Reviews", we added the statement to the title page and provided a signed copy in PDF format.

Comment #6

An informative, structured abstract of no less than 336 words should accompany each manuscript. The Abstract will be structured into the following sections and adhering to the word count thresholds indicated in parentheses:

AIM (no more than 20 words): The purpose of the study should be stated clearly and with no or minimal background information, following the format of: "To investigate/study/determine…"

METHODS (no less than 140 words): You should present the materials and methods used for all of the data presented in the proceeding Results section of the abstract.

RESULTS (no less than 150 words): You should present P values where appropriate. You must provide relevant data to illustrate how the statistical values were obtained, e.g. 6.92 ± 3.86 vs 3.61 ± 1.67, $P < 0.001$.

CONCLUSION (no more than 26 words): You should present your findings and implications that are within the scope of the data you have presented in the preceding Results section. The conclusion should be written in the present tense.

Authors' response: we edited the abstract accordingly.

Comment #7

Please offer the audio core tip, the requriment are as follows:

In order to attract readers to read your full-text article, we request that the first author make an audio file describing your final core tip. This audio file will be published online, along with your article. Please submit audio files according to the following specifications:

Acceptable file formats: .mp3, .wav, or .aiff

Maximum file size: 10 MB

To achieve the best quality, when saving audio files as an mp3, use a setting of 256 kbps or higher for stereo or 128 kbps or higher for mono. Sampling rate should be either 44.1 kHz or 48 kHz. Bit rate should be either 16 or 24 bit. To avoid audible clipping noise, please make sure that audio levels do not exceed 0 dBFS.

Authors' response: as requested, we recorded an audio core tip in mp3 format and added the text to the manuscript.

Comment #8

Please write the comments.

Writing requirements for each subsection

(1) Background

To summarize concisely and accurately the relevant background information so that readers may gain some basic knowledge about your study's relevance and understand its significance for the field as a whole.

(2) Research frontiers

To introduce briefly the current hotspots or important areas in the research field as related to your study.

(3) Innovations and breakthroughs

To summarize and emphasize the differences, particularly the advances, achievements, innovations and breakthroughs, as compared to other related or similar studies in the literature, which will allow the readers to assimilate the major points of your article.

(4) Applications

To summarize the practical applications of your research findings, so that readers may understand the perspectives by which this study will affect the field and future research.

(5) Terminology

To describe concisely and accurately any terms that may not be familiar to the majority of the readers, but which are essential for understanding your article.

Authors' response: we wrote the comments, following the editor's suggestions

REVIEWERS' COMMENTS

Reviewer #00004093

COMMENTS TO AUTHORS

This is a very interesting article. Please improve on following points.   There are too many abbreviations. Please limit the number of abbreviations.   This area of research can actually be called "molecular pathological epidemiology (MPE)". As a difference from typical MPE research that used molecular pathology analysis, in neurological and psychiatric fields, radiological imaging has been used. But basic principles, strengths and caveats remain the same. Thus, please discuss MPE. Here are references: S Ogino et al. Gut 2011; S Ogino et al. Mod Pathol 2013; A Nishi et al. Am J Prev Med 2015; PT Campbell et al. CEBP 2015; R Nishihara et al. Eur J Epidemiol. There is also an international meeting series (S Ogino et al. Cancer Causes Cont 2015).

Authors' response: We thank the Referee for his/her suggestion. In the revised manuscript we reduced the number of abbreviations. We also commented the concept of MPE in the discussion section.

Reviewer #02835073

COMMENTS TO AUTHORS

Good for publication.

Authors' response: We thank the Referee for his/her positive comment.

Other comments/requirements

Language revision: our English mother tongue coworker, Dr. Rita Santacroce, carefully polished the language, following the journal guidelines. We are therefore sure that our revised manuscript will reach a "Grade A" in language evaluation.

Plagiarism detection

Google Scholar search of the final title: as requested, we performed a check of our final title using Google Scholar. The search was conducted on November 5th 2015 and did not find any article with the same name in the web. We added a screenshot of the results in our "**Google Scholar file".**

Cross check analysis of the revised manuscript: our institution does not provide us with the suggested software "CrossCheck". We therefore used a similar and free plagiarism detection tool, called "Grammarly" (https://www.grammarly.com/plagiarism) and found no sign of plagiarism. We added a screenshot of the results in our "**cross check analysis file".**