Author’s response to reviews

Title: Change in the P300 Index - A Pilot Randomized Controlled Trial of Low-frequency Electrical Stimulation of Acupuncture Points in Middle-aged Men and Women.

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Version: 1 Date: 14 Mar 2017

Author’s response to reviews:

Reviewer 1.

1. To avoid misconception, electrical stimulation at acupoints should be described as points since this type of stimulation is different from acupuncture.

Re:→ Thank you for your suggestion. To avoid misconception, we added the notion of non-invasive stimulation to the introduction and method. However, in this study, 'acupuncture point' cannot be modified because it has important meaning in traditional medicine. The reason for choosing 'acupuncture point' is included in the discussion. 'Acupuncture point' is used for various stimuli such as moxibustion, acupressure, 'Acupuncture point' We think it is right to express.

2. The discussion that a male participant likely has higher work related stress than their counterpart should be substantiated with the lifestyle of the subjects enrolled in the study. How was stress determined? Were there non responders to the treatment? Was there a follow up on the effect after the stimulation? Was the effect long lasting?

Re:→ It is wrong to associate stress with work. The discussion on 'working stress' has been removed. And there was no follow up after the stimulation. (Line 291-296)

3. Line 37, page 1 of introduction: what does the word even mean in the context of the sentence?

Re:→ We modified the sentence. Line 60-64
4. Line 27, page 2 of introduction: the word solve should be replaced with reduced.
Re: We modified the word. (Line 82-88)

Reviewer 2.

1. English correction by native speakers is strongly recommended to improve the manuscript.
Re: We corrected by the manuscript by AJE. We attach the certificate.

Introduction

1. Relevant reference is needed to the sentences, e.g. 'Alternative medicine is easily accessed and inexpensive and is therefore a good method to solve the problem of senile brain disorders in an aging society.' I'm not sure whether the alternative medicine is indeed inexpensive than others or not. If yes, isn't it a special case in Asian countries? Furthermore, is there any evidence supporting the treatment effect of the alternative medicine, at least EA in this case, for brain disorders?
Re: We appreciate your advice. We have not considered global trends. Modified the manuscript to reflect your suggestion. And added reference to support the content. (Line 82-84)

2. In Introduction part, I'd like to suggest to provide the concrete rationale for this study. It is hard to get why the researchers performed the study.
Re: We modified the introduction. (Presented a concrete rationale to which this study should be conducted) (Line 82-94)

Methods

1. Considering the readers, it would be interesting point to prescribe the theoretical grounds for the selection of acupoints, duration, and frequency of EA.
Re: We modified it according to your suggestions. (Line 120-122)

2. Who performed the EA stimuli? A well-experienced and licensed Korean medicine doctor?
Re: Yes, we added content to the manuscript. (Line 117-120)

3. Which side of acupoints were chose? Left, right, or bilateral?
Re: Bilateral. We added content to the manuscript. (Line 118)
Results

1. Is there any reason for subgroup analysis based on gender? Any hypothesis before conducting the study? Any notable results between male and female groups from previous studies (references)?

Re: The reason is explained at the end of the introduction. References are also attached. And we also explained sex difference in the discussion part. (Line 91-94)

2. P300 latency and amplitude: Although p value is over 0.05 (0.057) when comparing the Pz channel signal between groups, it is still a marginally significant result which should be noted and also discussed.

Re: Thank you for your advice. We corrected table and result.

Discussion

1. The following sentence is meaningless or less of reference. If it is not closely related to the results of the study, it could be omitted. 'Modern people have more complicated daily lives than people in the past…'

Re: We deleted sentence.

2. Based on the survey results, the men had more frequent smoking and drinking experiences than the women, and this may have acted as a negative factor for the improvement of P300 amplitude. : Is this hypothesis confirmed by the data? For example, did you measure the participants' smoking and drinking behavior? If not, it is hardly supporting the results.

Re: We checked the participants' drinking and smoking status through questionnaires (Table 6). And we have attached a preliminary study on the effects of smoking and drinking on cognitive function.

Conclusion

1. This study confirmed that the amplitude of the P300, an index used to assess the cognitive function memory, increases in middle-aged women by observing the correlation between changes in the P300 and low-frequency electrical stimulation. : This sentence sounds too conclusive and does not provide a precise summary of the results.

Re: We modified the sentence. (Line 311-317)