Reviewer’s report

Title: Electroacupuncture upregulates ERK signaling pathways and promotes adult hippocampal neural progenitors proliferation in a rat model of depression

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Reviewer: Hee Young Kim

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Major Compulsory Revisions

Although this study is quite interesting that acupuncture can regulate depression through ERK-mediated stem cell proliferation, several critical points need to figure out to show positive effects of acupuncture, below;

In introduction: “several studies have indicated that EA raises the levels of these growth/neurotrophic factors [9]”. As Ref #9 did not mention EA, it is cited wrongly. In methods, “EA stimulation was performed at ‘Bai-Hui’ (Du-20) and ‘Yang-Ling-Quan’ (GB-34) acupoints. These two acupoints have been applied and showed some antidepressant effects in our preliminary and other studies [12-14].” ref #12 is wrong.

In methods, a critical point should be considered. EA was performed at ‘Du-20’ and ‘GB-34’. Du-20 is single point while GB34 is bilateral points. How do you connect a pair of needles to total three points? Du20-left GB34 and Du20-right GB34? Explain in detail how acupuncture was performed? i.e., anesthesia, how about electrical charges in acupoints, positive or negative charges. If electrical charges are connected like Du20 (+) and GB34 (-), it will make long flow thereby stimulating whole body. For short electrical flow and acupoints stimulation, refer “Pain 2008, Electroacupuncture-induced analgesia in a rat model of ankle sprain pain is mediated by spinal alpha-adrenoceptors”

For EA experiments, sham acupoints group should be included, to see if their effects are from electrical stimulation or acupoints-specific effects.

To show if signaling of ERK involved in proliferation of neural stem cell in stress conditions and it is recovered by EA, at least ERK expression in stress condition would be reduced significantly. But, there seems no difference in ERK between normal and stress groups.

Again, there are no significant differences in cell viability of PBS groups, neurosphere number or p-ERK between normal and model. To show any meaningful effects in acupuncture treatment, first of all, those factors should be different from normal values in stress model,

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