Reviewer's report

Title: Electroacupuncture activates corticotrophin-releasing hormone-containing neurons in the paraventricular nucleus of the hypothalammus to alleviate edema in a rat model of inflammation

Version: 2 Date: 1 February 2008

Reviewer: You Wan

Reviewer's report:

Comment

The submission of Li et al. demonstrated that electroacupuncture (EA) significantly decreased CFA-induced edema possibly through inhibition of ACTH in blood. Authors also tried to prove that this inhibition of EA was through NR1 phosphoralation of NMDA receptors in CRH-containing neurons of the paraventricular nucleus.

The research is of interest, but the reviewer has the following concerns.

Major concerns:

1. As stated by reference 5, electrical stimulation of the PVN significantly increased the pain threshold and enhanced acupuncture analgesia. But in the present study, author claimed that no involvement of ACTH was found in EA anti-hyperalgesic effect. How to explain this discrepancy?

2. ACTH (11-24) and astressin were injected intravenously. Could they enter into the brain (paraventricular nucleus)?

3. If ACTH (11-24) and astressin could penetrate brain-blood barrier, how authors exclude the possibility that ACTH takes role peripherally?

4. On page 5, â##CFA-inflamed rats were divided into three groups (n = 7 per group): 1) CFA + Vehicle + Sham EA, 2) CFA + Vehicle + EA, and 3) CFA + Astressin (Sigma) + EA.â## It seems that one more group â##CFA+Astressin+Sham EAâ## was ignored?

5. Although authors strongly suggested that there was no stress reaction in the present study, but under EA stimulation at intensity as high as 3 mA, stress should not be avoid completely. Authors could give out their opinion, but should not draw this conclusion absolutely. Please refer to relative references like Wan Y, et al., Acupuncture Research 2001; 26: 234-240.

6. Result of Fig. 6 should be added more in detail. In the text, author claimed that â##some neurons were single-labeled with CRH, suggesting that they were not activated by EAâ##. It is encouraged that authors count and give out the exact number or percentage of the double-stained neurons.

7. In Fig. 6, a bigger amplification to doubly stained neurons is suggested, for example a bigger amplification is inserted as an inset of Fig. 6A, B or C. In the
present picture, it is hard to see clearly the positive staining of a neuron.

8. Conclusion is simple and not supported strongly by authors' evidences. It is better to state like following: "Electroacupuncture (EA) significantly decreased CFA-induced edema through inhibition of ACTH in blood. This inhibition of EA was possibly through activation of NMDA receptors in CRH-containing neurons of the paraventricular nucleus." 

Minor concerns:
1. "3.1 EA increased plasma levels of ACTH" should be "3.1 EA increased plasma levels of ACTH in CFA rats"
2. Figure 1 axis should be "Time-point after CFA"
3. Page 10: "However, paw thickness in EA-treated rats plus ACTH (11-24) was no different from that in sham EA rats plus vehicle" should be "However, paw thickness in EA-treated rats plus ACTH (11-24) was not different from that in sham EA rats plus vehicle".

What next?: Accept after minor essential revisions

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