Peer Review File

Article information: https://dx.doi.org/10.21037/lcm-21-42

Review Comments

Reviewer 1: This article covers an interesting and important subject. However, it has limitations and needs a major revision:

#1: Severe language problems makes it difficult to read. In several sentences it is unclear what the authors refer to. I have marked just a few such unclarities, but the entire text needs a language revision.

Response: Dear reviewer, we appreciate your comment and correction. Our text has been updated and revised. We highlight all changes in blue.

#2: The Method section is too short. There is no reference to the method, data collection and data analysis is unclear.

Response: Dear reviewer, we appreciate your comment and correction. We would like to explain that the current manuscript was submitted as a "Narrative Review", that is, it describes and appraises previous work but does not describe specific methods by which the reviewed studies were identified, selected and evaluated (for more details: https:/ /guides.temple.edu/c.php?g=78618&p=3879604).

We know that narrative revisions have limitations, especially the biases that occur in selecting and assessing the literature, and that is why systematic reviews are currently more popular and performed by researchers. However, our intention in the actual manuscript was to show an overview of the topic, a more critically reflective or integrative kind of literature review product, which may help to justify further research on auriculotherapy.

Please note that, as requested, we have tried to improve the methodology description, so we have rewritten the item as follows:

“This narrative review began with a literature search using the PubMed/MEDLINE database, without restrictions regarding the year, for articles written only in English language including: Auricular Acupuncture OR Auriculotherapy AND Pain AND Neuromodulation OR Auricular Vagus Nerve Stimulation. A multidisciplinary group of researchers searched, reviewed and interpreted preclinical and clinical studies, as well as review studies. Searches were conducted until June and an update was performed in October 2021. Over 123 studies were found and 38 were included in this review. The articles were chosen according to their relevance to the purpose of the review based on the authors’ clinical and research experience in acupuncture and auriculotherapy.” (Page 4, Line 88-97).

#3: A Limitation-section is missing. Why only one data base? Are there limitations with the method? Can interesting articles have been missed?

Response: Dear reviewer, thank you for your suggestion. We included a paragraph in the discussion to talk about the limitations of our manuscript which included a single database and analysis of only publications written in English (Page 19, Line 407-416).

#4: References are referred to in an unclear way, and the authors often refer to secondary sources.
Response: Dear Reviewer, Thank you for your comment and correction. Our references have been revised (Page 22 Line 479-609).

#5: The first subtitle under “Results and discussion” is “Ear cartography and the neuroscientific perspective”. At least the first half fits better in the Introduction.
Response: Dear reviewer, we appreciate your observation and correction. We created a section specifically for the discussion (Page 18, Line 379) and changed the title and subtitle “Results and discussion” and ”Ear cartography and the neuroscientific perspective” to a title “Auricular cartography” (Page 5, Line 103). In this way we gave more coherence to the text, remaining in this section.

#6: The references are old and sometimes odd! In “Animal models” the references are from 1975, others are also more than 20 years old. It is more of a historical lesson than describing modern research.
Response: Dear reviewer, we greatly appreciate your remarks and useful suggestions. Our "Animal Models" section has been revised, and new references have been added. However, we do not only address modern research, we also believe that older research is relevant to a historical rescue (Page 12, Line 244-303).

#7: Add a figure of the auricular innervation.
Response: Dear reviewer, we appreciate your suggestion. We have included the suggested image (Page 7, Line 137) and two other images (Page 10, Line 201; Page 16, Line 337).

Reviewer 2: Here are the most important shortcomings:

#1: Under 'Author Contributions' it is stated that 4 of the 6 authors were responsible for the conception and the manuscript design. Unfortunately, the manuscript has no consistent concept and no relevant division at the moment, and there is no design at all. Where there are headings, the content and references do not match.
Response: Dear reviewer, we appreciate your comment and correction. We would like to inform you that we have revised the entire manuscript, changed the title of some sections and added a discussion section. We hope the changes we made will be sufficient to make the manuscript more context-appropriate. The authors' contribution is up to date (page 20, line 441-450).

#2: This is a very important point: there is almost always no primary literature cited but very often secondary literature (109 Nogier, 133 Nogier, and much more)

Response: Dear reviewer, we appreciate your comment. In the line 109, we have added a new reference (now page 8 line 169). However, in line 133, now page 7 and line 165, which cites the study by David Alimi, that corresponds to the primary reference.

#3: 90: The keywords are incomplete, auricular medicine and many other keywords are not even mentioned.
Response: Dear reviewer, we appreciate your comment and correction. The keywords have been updated (page 2, line 49,50).

#4: Results and discussion are not separated.
Response: Dear reviewer, we appreciate your comment and correction. We would like to inform you that these sections have been separated as requested.

#5: The historical lists are very often wrong and end suddenly with line 162. But we are only here in 2013. The most important research results on the subject are missing.
Response: We thank the reviewer for the comment. We recognize that some important works are missing. However, in historical terms, our review follows the same chronological order as the references below:

- HOU, P.W. et al. The History, Mechanism, and Clinical Application of Auricular Therapy in Traditional Chinese Medicine. Evid Based Complement Alternat Med. 2015;495684.
- WIRZ-RIDOLFI, A. The History of Ear Acupuncture and Ear Cartography: Why Precise Mapping of Ear Points Is Important. Acupuncture 2019; 31(3):145–156.
- RABISCHONG, P. et al. Scientific Basis of Auriculotherapy: State of the Art. Med Acupunct. 2014;26(2):84-96.

In addition, we have added historical facts and works, such as Dr. T. Olsen, and information from WFAS.

#6: Under the 'animal models' section, there are references to the literature that are not at all related to it (e.g., Ref 21, 22 and many more).
Response: You are absolutely correct in your remark. We appreciate this comment and changes have been made.
We modified the paragraph: “Nogier's publications assisted in the further search for locations of auriculotherapy points. The auricular points were verified in clinical applications and in animal experiments. With the results of these researches, a complete map of the body image in the ear was developed and confirmed in the following years in humans (21, 22)”. Adjusting the text as follows: “The auricle in humans and other mammals has a special anatomical structure, that is, there is a branch of the vagus nerve distributed in the shell (Zhang et al, 2012; Chung et al, 2011). In fact, most of the information about the

anatomy of the vagus nerve and its projections was discovered by tracing the vagus nerve in rats and is generally considered to be similar to humans (Chung et al, 2011)." (page 12, line 251-256)

Furthermore, a new paragraph has been added: "Gao et al. (2008) systematically analyzed the location specificity and response characteristics of autonomic changes using different stimulation methods in auricular acupuncture in rats. The authors showed that stimulation of the auricle with either manual or electroacupuncture (100 Hz–1 mA) was able to decrease blood pressure, causing bradycardia and gastric contraction. The study suggested that the inferior concha is the most powerful site for regulation of autonomic functions, at least in animals (Gao et al, 2008)." (page 13, line 270-276)

References:

GAO, X. Y. et al. Investigation of specificity of auricular acupuncture points in regulation of autonomic function in anesthetized rats. Auton Neurosci. 2008 Feb 29;138(1-2):50-6. doi: 10.1016/j.autneu.2007.10.003. / ZHAO, Y.X. et al. Transcutaneous auricular vagus nerve stimulation protects endotoxemic rat from lipopolysaccharide-induced inflammation. Evid Based Complement Alternat Med. 2012;2012:627023. doi: 10.1155/2012/627023. / CHUNG, W. Y. et al. Peripheral muscarinic receptors mediate the anti-inflammatory effects of auricular acupuncture. Chin Med . 2011 Jan 21;6(1):3. doi: 10.1186/1749-8546-6-3.

#7: Only one database was searched. What about many others, e.g. CNKI. The authors say it is a 'Chinese method'. Wouldn't it be obvious to look into these databases as well?

Response: Dear reviewer, we appreciate your comment and correction. We would like to inform you that your observations have been cited as limitations and included in the discussion (Page 19, Line 407-416).

#8: Numerous articles cited in the text do not appear in the reference list at all: e.g., 241; Bailey and Bremer, Dell and Olson, etc. etc.

Response: Dear Reviewer, Thank you for your comment and correction. Our references have been revised (Page 22 Line 479-609).

#9: The Nogier reflex that is so important with ear acupuncture is not even mentioned.

Response: Dear reviewer, we appreciate your comment. Your suggestion was included (Page 10, Line 208-213).

#10: Numerous European and Chinese, but also American studies on ear acupuncture and neuromodulation are missing.

Response: Dear reviewer, we greatly appreciate your remarks and useful suggestions. New studies were included throughout the text and we also added a paragraph to address our limitations, which included the lack of some studies (Page Page 19, Line 407-416).