



OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-20-00193

Title: Massage Therapy Related Brain Plasticity in the Treatment of Peripheral Nerve Injury: A Resting-state fMRI Study in Rats

Reviewer's Name: Michele R Colonna

Reviewer's country: Italy

Date sent for review: 2020-3-17

COMMENTS TO AUTHORS

This is an interesting novel application of stimulation of brain plasticity through massage after peripheral nerve injury. The idea sounds original, methods are well-documented and fMRI looks a very sensitive tool even in small animals. The Authors highlight the scientific bases of the application but the discussion looks disproportionate, with too short conclusions. Weak points are well-highlighted.

OPEN PEER REVIEW REPORT 2

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-20-00193

Title: Massage Therapy Related Brain Plasticity in the Treatment of Peripheral Nerve Injury: A Resting-state fMRI Study in Rats

Reviewer's Name: Gabriele Siciliano

Reviewer's country: Italy

Date sent for review: 2020-3-17

COMMENTS TO AUTHORS

In this work, the author explores the role of massage therapy in recovery of functions after peripheral nerve injury (PNI), evaluating the relationship between massage and brain plasticity, assessed by a fMRI parameter, namely ALFF.

There are some concerns that require attention.

Introduction

1) At the end of this sections the author briefly explain the mechanism underlying ALFF index and its role in experimental studies, also mentioning that is not applicable to human being in the evaluation of pre-injury states; maybe the author would like to better explain what this last affirmation means, also in the light of the design and the results of this work.

Material and methods

1) I hardly understand the division into the four groups. I would like to suggest to the author to be more specific in the definition of each group, adding in the text the same distinction reported in Table 1.

2) I noticed that there is not a group composed by normal animals submitted to massage: maybe the author would like to explain why she/he chose not to assess the effect of massage also in non-injured animals.

Discussion

1) In the first paragraph, the author compares the result obtained in massage group and model one, but such observations seem to be written as there was a basal fMRI scan, in addition to the 4-weeks fMRI

(Decreased ALFF was noted in the somatosensory cortex contralateral to the affected hindlimb after PNI, indicating suppressed spontaneous activity of the corresponding cortex. Then, the ALFF of contralateral somatosensory cortex significantly increased following a 4-week massage therapy over the reinnervated muscle, demonstrating restoration of neuronal activity).

Maybe the author would like to better clarify that his/her results are obtained from a cross-sectional assessment and not from a longitudinal one. At the same time, it could be explained why a baseline fMRI was not performed, in order to compare the acute cortical consequences of PNI with the evidences obtained after 4 weeks.

2) The aims of this work was to evaluate the role of massage in stimulating the recovery of brain activity; nevertheless massage is here proposed as a possible non-pharmaceutical treatment for PNI, but the author does not show any data about the animals motor-sensitive recovery after PNI, neither a correlation between the degree of recovery and ALFF variation is shown.

OPEN PEER REVIEW REPORT 3

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Title: Massage Therapy Related Brain Plasticity in the Treatment of Peripheral Nerve Injury: A Resting-state fMRI Study in Rats

Reviewer's Name: Yu Lei

Reviewer's country: China

Date sent for review: 2020-3-17

COMMENTS TO AUTHORS

In this study, the authors reported the dynamic brain plasticity of peripheral nerve injury (PNI) subjects treated by massage. Massage therapy is an important component of non-drug treatments in Traditional Chinese Medicine. According to the literature, little is known about the functional and structural plasticity in brain after massage therapy. The study is interesting and well-designed. However, a few problems should be addressed and this may help the reader to have a deeper understanding of this manuscript.

In introduction, pathophysiological mechanisms underlying massage effect on PNI subjects in this research should be better discussed.

In Methods, why only female rats were involved in this experiment?

Although the authors has explained why the fMRI scans were not collected before peripheral nerve injury, it is important to collect such data for investigating time effects and reducing individuals difference of the study.

In the section of fMRI data preprocessing, the authors did not describe whether or not they remove the several time points from the beginning? The description of normalization (or registration) part should be rephrased, many details were not clear, what's the standard template?

It could be interesting if the authors provide a correlation analysis between behavior assessments and ALFF values at specific brain regions. Is there any information at the acute period after PNI? e.g. at 1 week after PNI? If not, the authors should discuss these issues as limitations in Discussion.