Author's response to reviews

Title: Association of extracellular signal-regulated kinase expression with anti-allodynic effect in spared nerve injury rats by applying immediate pulsed radiofrequency

Authors:

Chun-Chang Yeh (anes2yeh@gmail.com)
Zhi-Fu Wu (aneswu@gmail.com)
Jui-Chieh Chen (yun197009@gmail.com)
Chih-Shung Wong (w82556@gmail.com)
Chi-Jung Huang (science.man2@gmail.com)
Jinn-Shyan Wang (fjmedwang@gmail.com)
Chih-Cheng Chien (chiencmail@gmail.com)

Version: 2 Date: 15 January 2015

Author's response to reviews: see over
Dear editors,

Here, we submit a manuscript entitled “Association of extracellular signal-regulated kinase expression with anti-allodynic effect in spared nerve injury rats by applying immediate pulsed radiofrequency” for consideration to be published in the *BMC anesthesiology*. Neither this manuscript nor any significant part of it is under consideration for publication elsewhere, or has appeared elsewhere in a manner that could be constructed as a prior or duplicate publication of the same, or very similar work. We look forward to seeing this manuscript to be accepted for publication in your high quality journal.

Applying pulsed radiofrequency (PRF) close to the dorsal root ganglion (DRG), or peripheral nerves has been demonstrated effectively in the treatment of chronic neuropathic pain conditions. The mechanism of analgesic effect of PRF treatment remains uncertain. PRF application at DRG may alter the biological actions on synaptic transmission, cell morphology, and Fos expression in the superficial dorsal horn of the spinal cord with trivial effect on nerve tissue. Multiple evidence show that inhibition of ERK activation may be a promising therapeutic target for the treatment of neuropathic pain. In our study, we examined the analgesic effect of PRF treatment with usual clinical setting (PRF waves of 500 kHz frequency, 45 or 60 volt (V) output, 20 millisecond pulse width for 6 min treatment) and the relationship between PRF and ERK1/ERK2 expression in spinal cord dorsal horn in SNI rats.

The study reported that the immediate PRF treatment after SNI significantly alleviated the mechanical and cold allodynia in the SNI rats. For both the PRF 45 V and 60 V six-minute treatments, mechanical allodynia and cold hypersensitivity were reduced during the 28-day observation. Furthermore, there were no observable differences of results between the PRF 45 V and 60 V treatment groups. In addition,
the activation of extracellular signal-regulated kinase 1 and 2 (ERK1/2 in ipsilaterally spinal dorsal horn of SNI rats was effectively inhibited in SNI+PRF-45V group for 28 days post-surgery.

As a result, we concluded that immediate PRF application treatment on proximal nerve injury site provided a significant inhibition of neuropathic pain formation, accompanied by an inhibition of ERK activation. For clinical translation, well-designed randomized controlled trials are required to identify the beneficial effect of PRF treatment proximal to the nerve injured site. Further studies on the effect of PRF in the expression of ERK deserve additional elucidation to provide rationale in treating neuropathic pain.

The corresponding author is empowered by all of the authors to act on their behalf with respect to the submission of the manuscript; that authors have taken due care to ensure the integrity of the work. Both of the corresponding authors have equal contributions to the study, conducting the design, the process, the discussion, the analysis, and the editing of this manuscript.

Sincerely Yours,

Jinn-Shyan Wang¹, PhD, and Chih-Cheng Chien¹, ², MD, PhD

Professor¹, ²
¹School of Medicine, Fu Jen Catholic University, 510, Chung-Cheng Rd., New Taipei City 24205, Taiwan
¹, ²Department of Anesthesiology, Cathay General Hospital, Taipei, Taiwan

Competing Interests

The authors declare that they have no conflict of interest.

Authors’ contributions

CC Yeh: helps conceive the study, conducted experiments, analyzed data, and wrote the manuscript; CC Chien & JS Wang: designed and supervised the study, analyzed
and explained data, as well as wrote the manuscript; ZF Wu: conducted animal study and analyzed and explained data; JC Chen: conducted molecular experiment, analyzed, explained data and wrote the manuscript; CJ Huang: Helped conceive the study, conducted experiment, statistical analysis and wrote the manuscript; CS Wong: conceived the study, analyzed data and wrote the manuscript. All authors read and approved the final manuscript.

**Funding**

The work was supported, in part, by the National Science Council (grant no. NSC 100-2314-B-016-002) and the Ministry of National Defense. (grant no. DOD98-05-04), Taipei, Taiwan, Republic of China.

**Author details**

1 School of Medicine, Fu Jen Catholic University, New Taipei City 24205, Taiwan

2 Department of Anesthesiology & Integrated Pain Management Center, Tri-Service General Hospital and National Defense Medical Center, Taipei, Taiwan

3 Graduate Institute of Cancer Biology, College of Medicine, China Medical University, No.91, Hsueh-Shih Rd., Taichung 40402, Taiwan

4 Department of Medical Research, Cathay General Hospital, Taipei, Taiwan

5 Department of Anesthesiology, Sijihih Cathay General Hospital, Sijih District, New Taipei City, Taiwan

6 Department of Anesthesiology, Cathay General Hospital, Taipei, Taiwan

7 Department of Biochemistry, National Defense Medical Center, Taipei, Taiwan
*Contributed equally

Corresponding authors: Jinn-Shyan Wang, PhD, and Chih-Cheng Chien, MD, PhD,

School of Medicine, Fu-Jen Catholic University, New Taipei City 24205, Taiwan,

R.O.C.