

# Electroacupuncture Alleviates Neuropathic Pain and Negative Emotion in Mice by Regulating Gut Microbiota [Letter]

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## Dear editor

I read with great interest an article published in the Journal of Pain Research titled “Electroacupuncture alleviates neuropathic pain and negative emotion in mice by regulating gut microbiota”.<sup>1</sup> Various behavioral tests and 16S ribosomal DNA (rDNA) sequencing in this study found that electroacupuncture can regulate intestinal flora and relieve chronic pain, and intestinal flora was recommended as a potential therapeutic target. This study is clinically valuable as it introduces new perspectives, and advances the field. However, extrapolating these research results and the experimental design has limitations and requires further verification and refinement to improve accuracy.

First, this study used only male C57BL/6 mice and did not consider the influence of sex on chronic pain management. Previous studies have revealed differences in the mechanism of chronic pain between the sexes at the genetic, molecular, cellular, and systemic levels.<sup>2</sup> Chronic pain is more prevalent in females and is more likely to be accompanied by depression. If EA has different effects in females, the research conclusions may not be applicable to clinical settings. Therefore, future research should include more female mice in the experimental group to verify whether EA has sex-specific effects and improve its clinical applicability. Second, the study examined uncontrolled dietary factors, and differences feed composition may have interfered with the experimental results and affected flora composition. In the high-fat diet group, mechanical hypersensitivity was obviously prolonged, and spontaneous pain generally increased.<sup>3</sup> In the later stage, all mice should be fed with standardized feed with the same composition, and dietary intake should be recorded to reduce the confounding effects of diet on gut flora changes. Finally, although this study confirmed that EA can regulate flora and relieve pain and emotional disorders, whether this occurs through the neurotransmitter system remains unclear. Previous studies have shown that intestinal flora can affect central nervous system function by regulating neurotransmitter levels and affecting neuronal activity. For example, sterile mice often exhibit anxiety and reduced levels of neurotrophic factors in the amygdala and hippocampus.<sup>4</sup> However, this study lacks direct neurobiological evidence, such as the determination of neurotransmitters in key brain regions, such as the amygdala, prefrontal cortex, and spinal cord. Future research should combine immunohistochemistry, ELISA, and molecular biological detection to systematically evaluate whether EA affects neurotransmitter-related signaling pathways and further clarify the connection between intestinal flora and the nervous system.

This study provides a valuable direction for relieving neuropathic pain and its accompanying negative emotions. However, its limitations still need to be addressed. Future researchers in related fields should optimize experimental designs and clinical transformation applications, develop animal models that better reflect clinical practice, and strengthen the in-depth verification of biological mechanisms to enhance the extrapolation of research. These improvements will further advance research and applications, effectively improving patients' neuropathic pain and negative emotional symptoms.

## Disclosure

The author reports no conflicts of interest in this communication.

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