

Electroacupuncture alleviates stress-induced visceral hypersensitivity through an opioid system in rats.

[Zhou YY](#), [Wanner NJ](#), [Xiao Y](#), [Shi XZ](#), [Jiang XH](#), [Gu JG](#), [Xu GY](#).

Source

Yuan-Yuan Zhou, Ying Xiao, Xing-Hong Jiang, Guang-Yin Xu, Institute of Neuroscience and Department of Neurobiology, Key Laboratory of Pain Research and Therapy, Soochow University, Suzhou 215123, Jiangsu Province, China.

Abstract

AIM:

To investigate whether stress-induced visceral hypersensitivity could be alleviated by electroacupuncture (EA) and whether EA effect was mediated by endogenous opiates.

METHODS:

Six to nine week-old male Sprague-Dawley rats were used in this study. Visceral hypersensitivity was induced by a 9-d heterotypic intermittent stress (HIS) protocol composed of 3 randomly stressors, which included cold restraint stress at 4 °C for 45 min, water avoidance stress for 60 min, and forced swimming stress for 20 min, in adult male rats. The extent of visceral hypersensitivity was quantified by electromyography or by abdominal withdrawal reflex (AWR) scores of colorectal distension at different distention pressures (20 mmHg, 40 mmHg, 60 mmHg and 80 mmHg). AWR scores either 0, 1, 2, 3 or 4 were obtained by a blinded observer. EA or sham EA was performed at classical acupoint ST-36 (Zu-San-Li) or BL-43 (Gao-Huang) in both hindlimbs of rats for 30 min. Naloxone (NLX) or NLX methiodide (m-NLX) was administered intraperitoneally to HIS rats in some experiments.

RESULTS:

HIS rats displayed an increased sensitivity to colorectal distention, which started from 6 h (the first measurement), maintained for 24 h, and AWR scores returned to basal levels at 48 h and 7 d after HIS compared to pre-HIS baseline at different distention pressures. The AWR scores before HIS were 0.6 ± 0.2 , 1.3 ± 0.2 , 1.9 ± 0.2 and 2.3 ± 0.2 for 20 mmHg, 40 mmHg, 60 mmHg and 80 mmHg distention pressures, respectively. Six hours after termination of the last stressor, the AWR scores were 2.0 ± 0.1 , 2.5 ± 0.1 , 2.8 ± 0.2 and 3.5 ± 0.2 for 20 mmHg, 40 mmHg, 60 mmHg and 80 mmHg distention pressures, respectively. EA given at classical acupoint ST-36 in both hindlimbs for 30 min significantly attenuated the hypersensitive responses to colorectal distention in HIS rats compared with sham EA treatment [AWRs at 20 mmHg: 2.0 ± 0.2 vs 0.7 ± 0.1 , $P = 4.23 \times 10^{-4}$; AWRs at 40 mmHg: 2.6 ± 0.2 vs 1.5 ± 0.2 , $P = 0.00163$; AWRs at 60 mmHg: 3.1 ± 0.2 vs 1.9 ± 0.1 , $P = 0.003$; AWRs at 80 mmHg: 3.6 ± 0.1 vs 2.4 ± 0.2 , $P = 0.0023$; electromyographic (EMG) at 20 mmHg: 24 ± 4.7 vs 13.8 ± 3.5 ; EMG at 40 mmHg: 60.2 ± 6.6 vs 30 ± 4.9 , $P = 0.00523$; EMG at 60 mmHg: 83 ± 10 vs 39.8 ± 5.9 , $P = 0.00029$; EMG at 80 mmHg: 94.3 ± 10.8 vs 49.6 ± 5.9 , $P = 0.00021$]. In addition, EA at the acupuncture point BL-43 with same parameters did not alleviate

visceral hypersensitivity in HIS rats. EA in healthy rats also did not have any effect on AWR scores to colorectal distention at distention pressures of 20 and 40 mmHg. The EA-mediated analgesic effect was blocked by pretreatment with NLX in HIS rats [AWR scores pretreated with NLX vs normal saline (NS) were 2.0 vs 0.70 ± 0.20 , 2.80 ± 0.12 vs 1.50 ± 0.27 , 3 vs 2.00 ± 0.15 and 3.60 ± 0.18 vs 2.60 ± 0.18 for 20 mmHg, 40 mmHg, 60 mmHg and 80 mmHg; $P = 0.0087$, 0.0104 , 0.0117 and 0.0188 for 20, 40, 60 and 80 mmHg, respectively]. Furthermore, EA-mediated analgesic effect was completely reversed by administration of m-NLX, a peripherally restricted opioid antagonist (EMG pretreated with m-NLX vs NS were 30.84 ± 4.39 vs 13.33 ± 3.88 , 74.16 ± 9.04 vs 36.28 ± 8.01 , 96.45 ± 11.80 vs 50.19 ± 8.28 , and 111.59 ± 13.79 vs 56.42 ± 8.43 for 20 mmHg, 40 mmHg, 60 mmHg and 80 mmHg; $P = 0.05026$, 0.00034 , 0.00005 , 0.000007 for 20 mmHg, 40 mmHg, 60 mmHg and 80 mmHg, respectively).

CONCLUSION:

EA given at classical acupoint ST-36 alleviates stress-induced visceral pain, which is most likely mediated by opioid pathways in the periphery.