Diuted bee venom injection into feng fu acupoint reduces facial and hind paw hypersensitivities and TNC C-OS expression in a Nitroglycerin (NTG)-induced migraine mouse model

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We recently reported that different peripheral hypersensitivities developed in the face versus hind paw in itroglycerine(NTG)-induced migaine mice model. We have also reported that diluted bee venom(DBV) into acupoint produced significant anti-nociceptive effects in several pain models. Here, we show that DBV injection into different acupoints reduces facial or hind paw hypersensitivity and the c-Fos expression in trigeminal nucleus caudalis(TNC) in repetitive NTG-injected mice. NTG(10 mg/kg) was administrated every other day for nine days. DBV(0.1 mg/kg) was subcutaneously injected into the Zusanli(ST36) or He gu(LI4) or Feng fu(GV16) acupoint 75 min after each NTG injection. Two hour after NTG injection, mechanical and cold sensitivity in hind paw and facial region was quantified. The immunohistochemistry for c-FOS expression was performed in TNC after the last NTG injection. Repetitive NTG injection developed the facial cold allodynia and hindpaw mechanical allodynia, and c-FOS expression significantly increased in TNC. DBV treatment into Zusanli or He gu acupoint did not suppress either NTG-induced hind paw mechanical allodynia or facial cold allodynia, while DBV injection into Feng fu acupoint completely blocked these hypersensitivities. The number of c-FOS positive cells was decreased in the Feng fu acupoint DBV-treated groups, but not other acupoint DBV-treated groups. Pretreatment with naloxone(5mg/kg, i.p.), an opioid receptor antagonist, did not reverse these anti-allodynic effects of DBV into Feng Fu acupoint, whereas yohimbine(5mg/kg, i.p.), an alpha2-adrenoceptor antagonist, completely blocked the effects of Feng Fu acupoint DBV. Moreover, the expression of c-FOS positive cells was restored only in the yohimbine pretreated DBV group. These findings demonstrate that DBV treatment into Feng Fu acupoint considerably decreased the repeated NTG-induced facial and hind paw hypersensitivities as well as the c-Fos expression. Furthermore, Feng Fu acupoint DBV-induced suppression of these migraine-like responses is closely associated with the activation of alpha-2 adrenoceptors, but not opioid receptors.