

Diluted bee venom injection into Feng Fu acupoint reduces facial and hind paw hypersensitivities and TNC c-Fos expression in a nitroglycerin-induced migraine mouse model

Sol-Ji Kim, Ji-Hee Yeo, Dae-Hyun Roh*

Department of Oral Physiology, School of Dentistry, Kyung Hee University, Seoul, Rep. of Korea.

INTRODUCTION

Migraine, a multifactorial primary headache disorder, is characterized by one-sided, severe, and pulsatile headaches. However, the pathophysiological mechanisms underlying migraine-associated peripheral hypersensitivities are unknown. Nitroglycerin (NTG), a nitric oxide donor and effective vasodilator, is generally used to induce migraine-like response in animals. We recently reported that different peripheral hypersensitivities developed in the face versus hind paw regions in repetitive NTG-treated mice. 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

MATERIALS AND METHODS

1. Animals

- C57BL/6 mouse (25-30g; DBL Co., Korea)

2. Drug Administration

- Nitroglycerin (NTG) : 10 mg/kg, *i.p.*

- NTG was repetitively injected every other day for 9 days

- DBV (Diluted bee venom) : 0.1mg/kg, *s.c.*, was injected in Zusanli (ST36) or Hegu (L14) or Feng fu (GV16) acupoint 75 min after each NTG injection.

- Naloxone (opioid receptor antagonist) : 5mg/kg, *i.p.*

- Yohimbine (alpha2-adrenoceptor antagonist) : 5mg/kg, *i.p.* was injected 30 min before DBV (feng fu acupoint) injection.

3. Peripheral hypersensitivity tests

- Mechanical allodynia, cold allodynia and thermal hyperalgesia

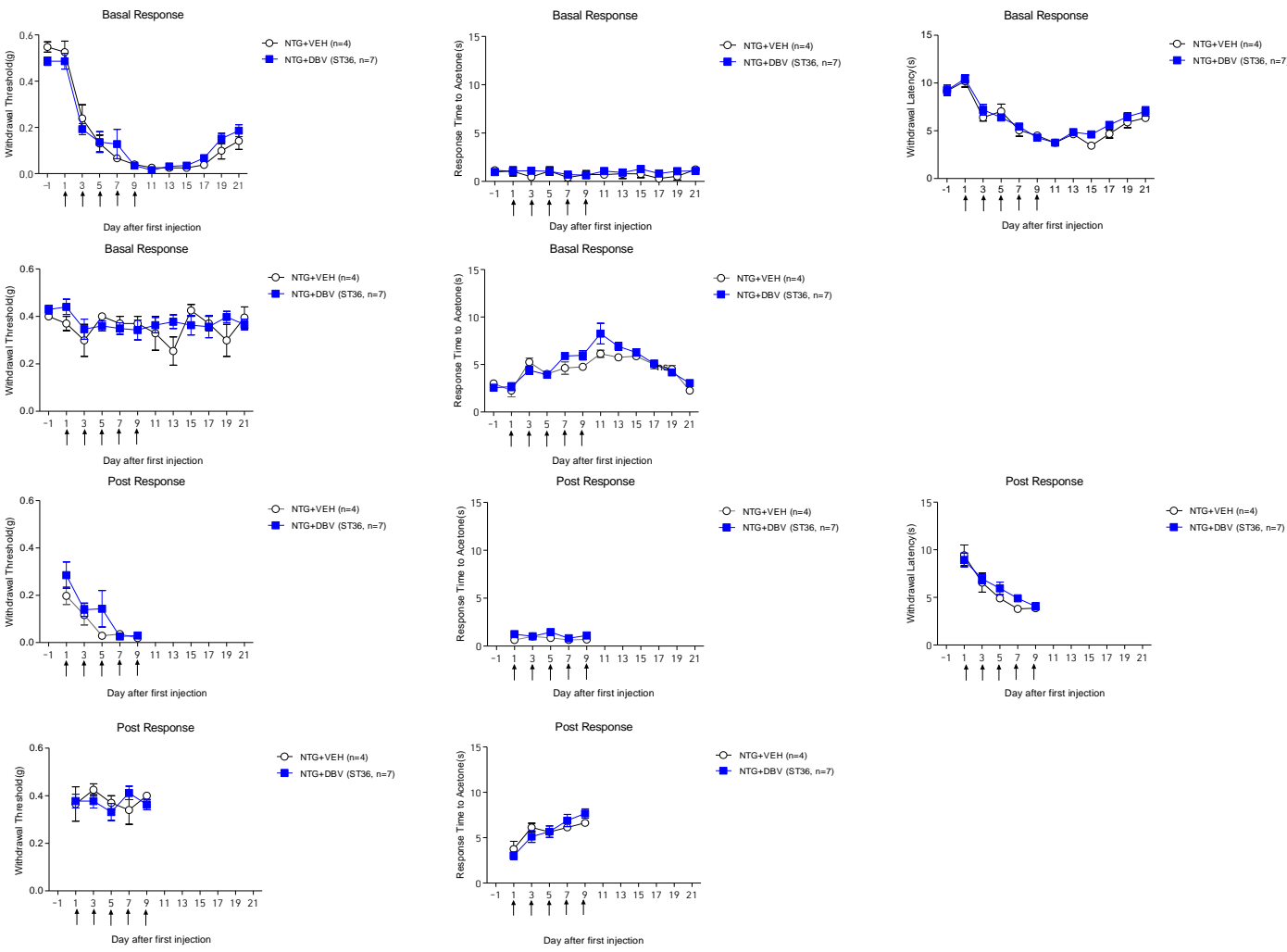
- Tests were performed prior and 2 hours after NTG injection.

4. Fos immunohistochemistry in trigeminal nucleus caudalis (TNC)

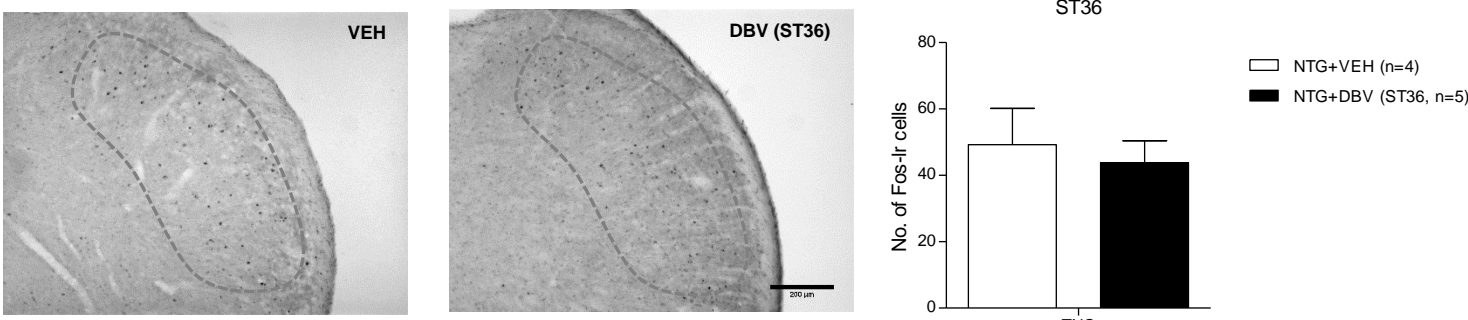
- primary Ab : Fos (Santa Cruz, 1:1000)

RESULTS

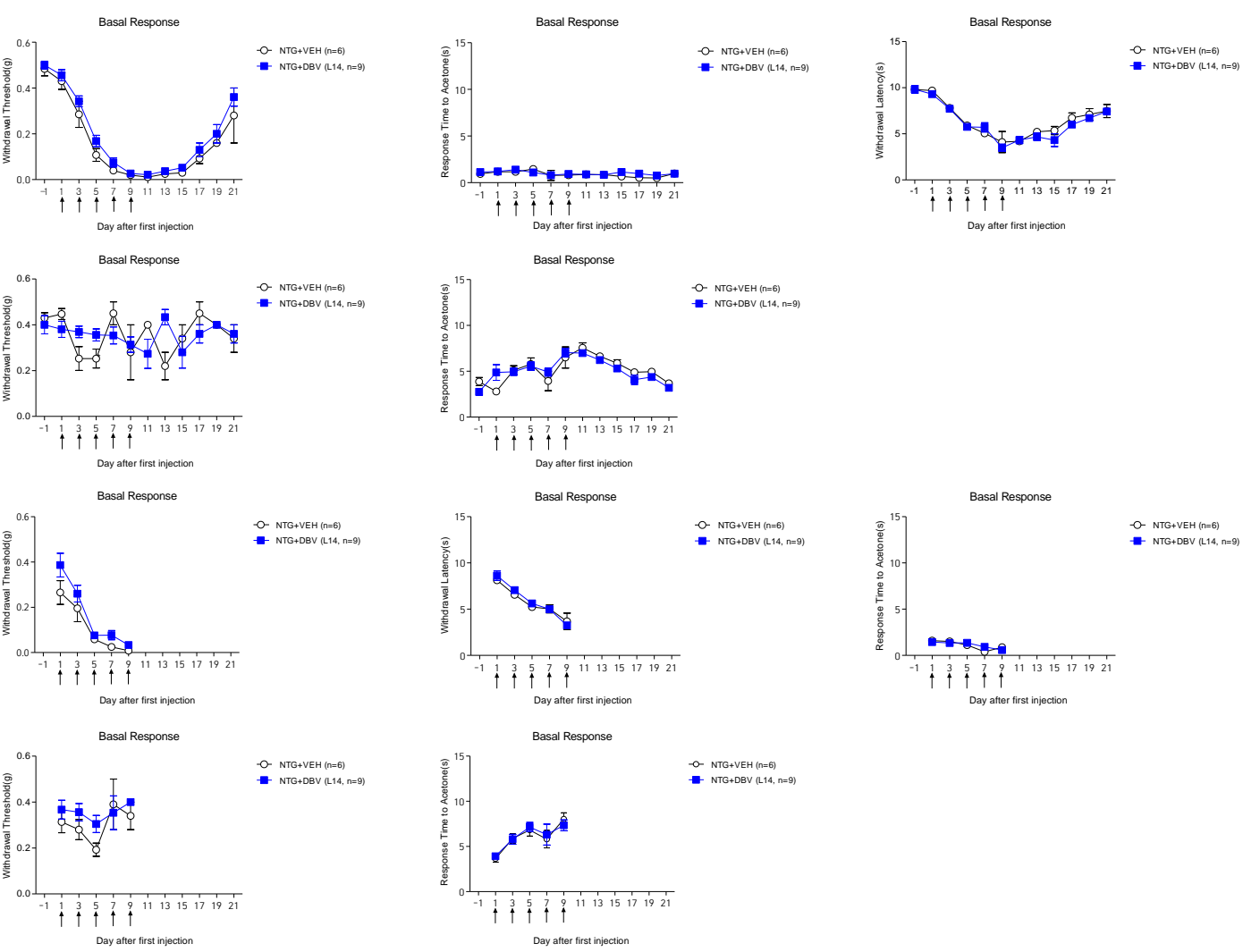
1. Effect of DBV treated into Zusanli acupoint on NTG-induced hind paw and facial hypersensitivities



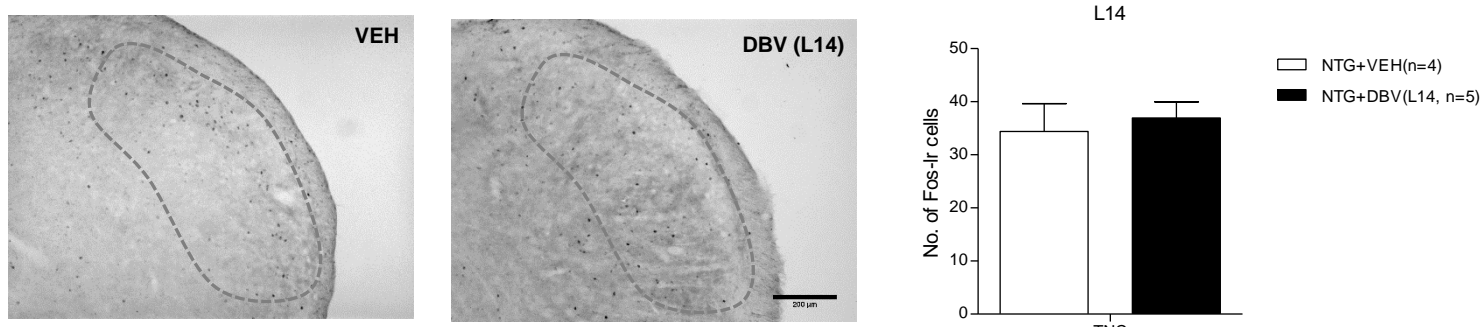
2. Effect of DBV treated Zusanli acupoint on NTG-induced Fos expression in TNC



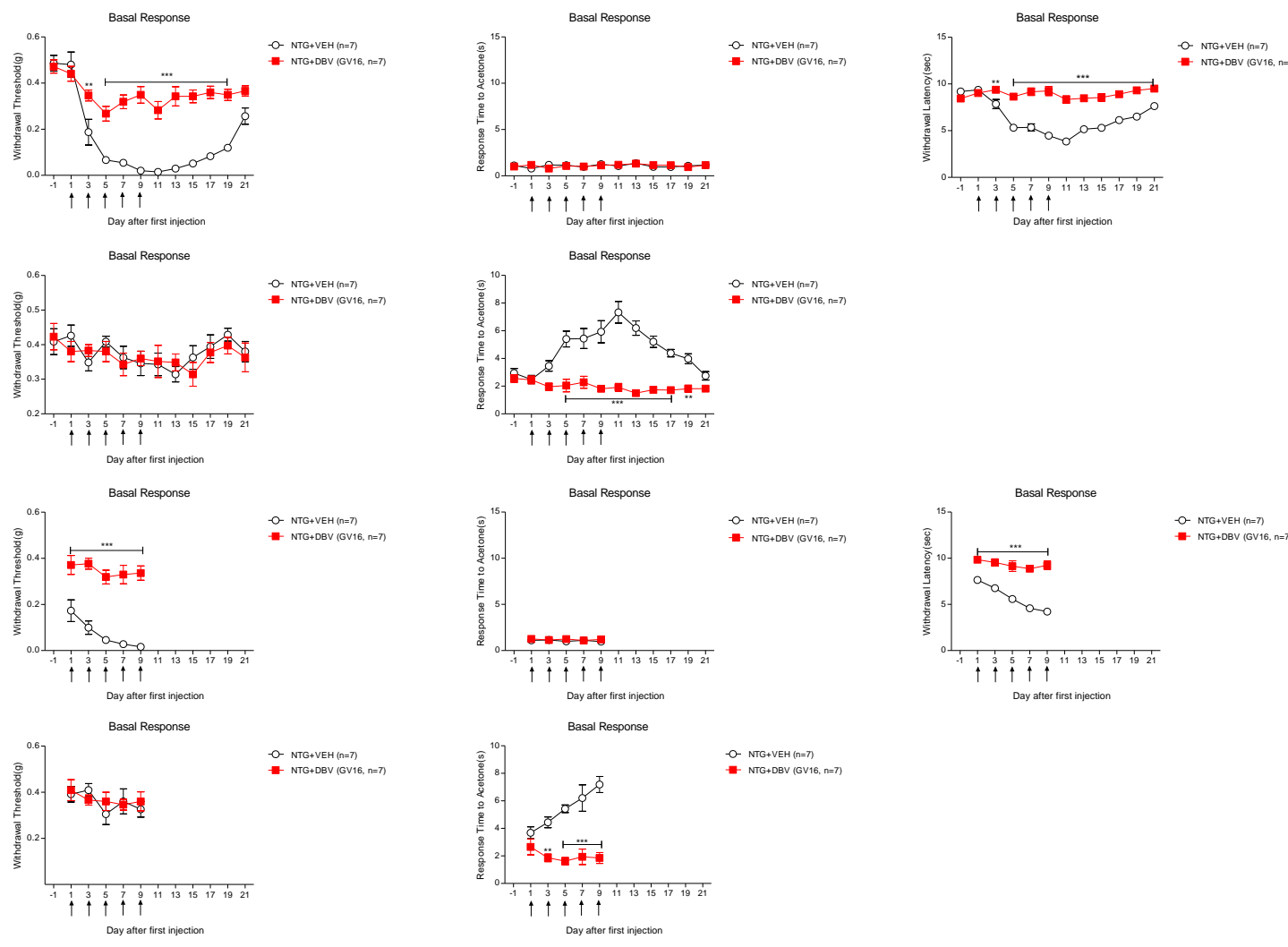
3. Effect of DBV treated into Hegu acupoint on NTG-induced hind paw and facial hypersensitivities



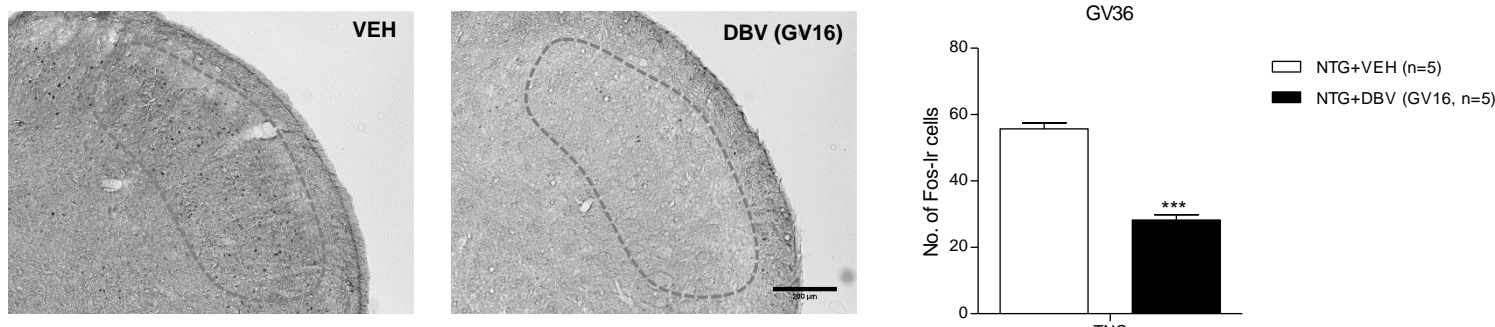
4. Effect of DBV treated into Hegu acupoint on NTG-induced Fos expression in TNC



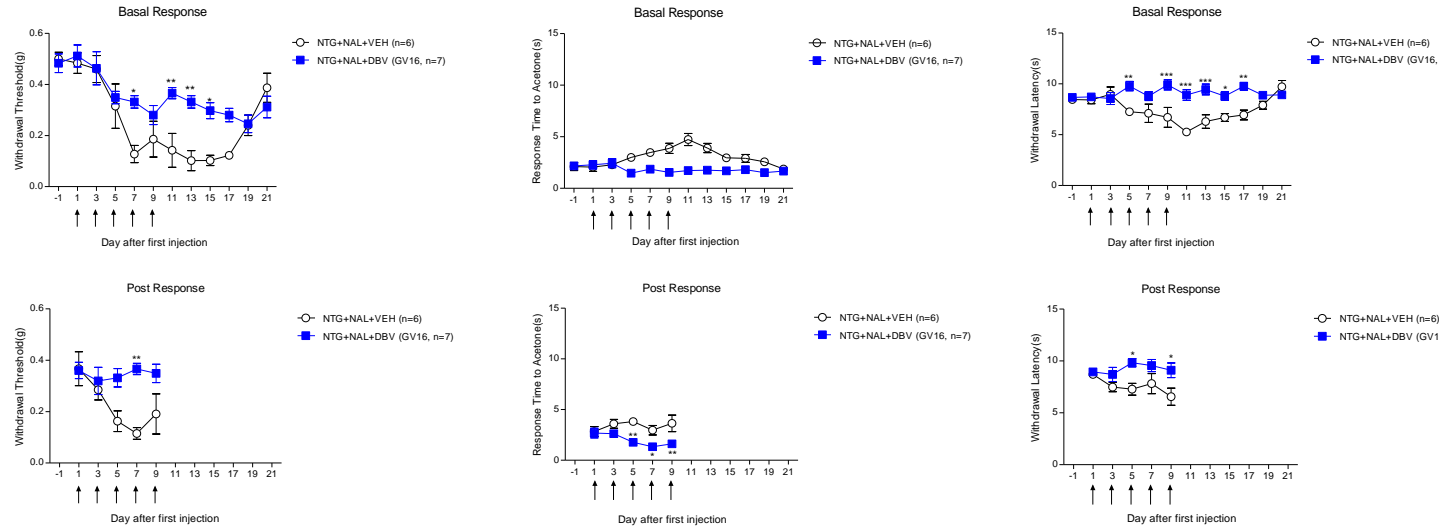
5. Effect of DBV treated into Feng fu acupoint on NTG-induced hind paw and facial hypersensitivities



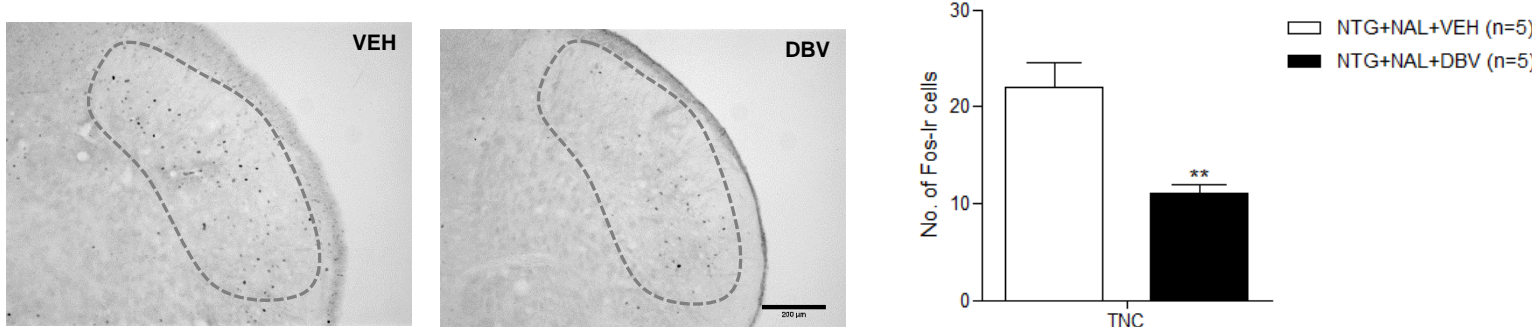
6. Effect of DBV treated into Feng fu acupoint on NTG-induced Fos expression in TNC



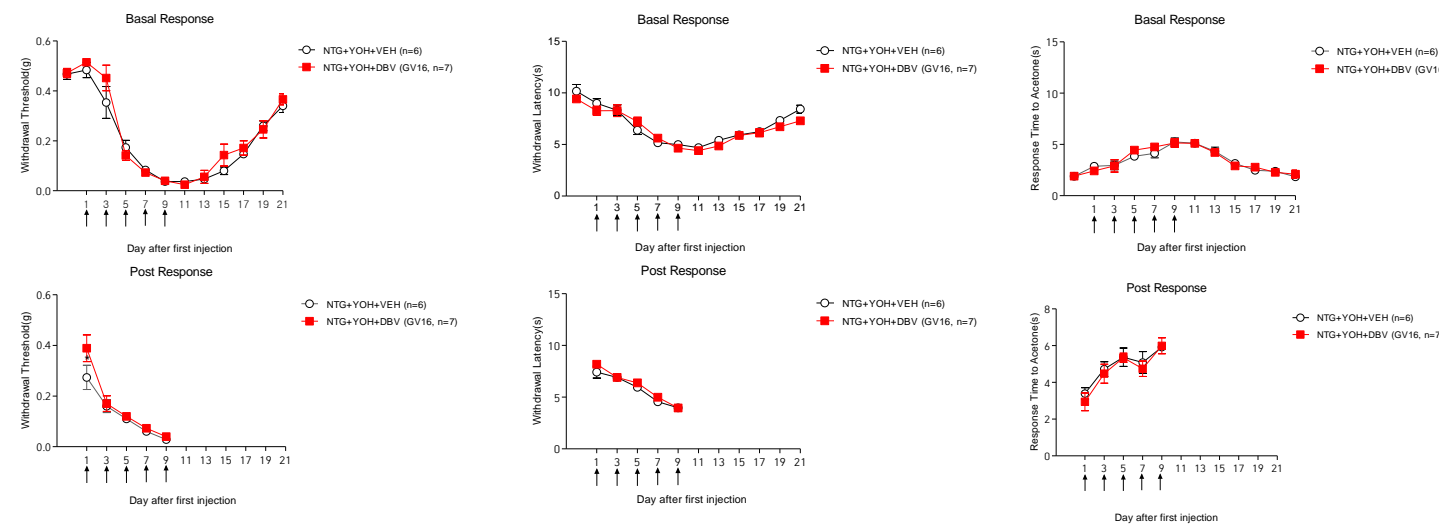
7. Involvement of opioid receptor on DBV treated into Feng fu acupoint Effect



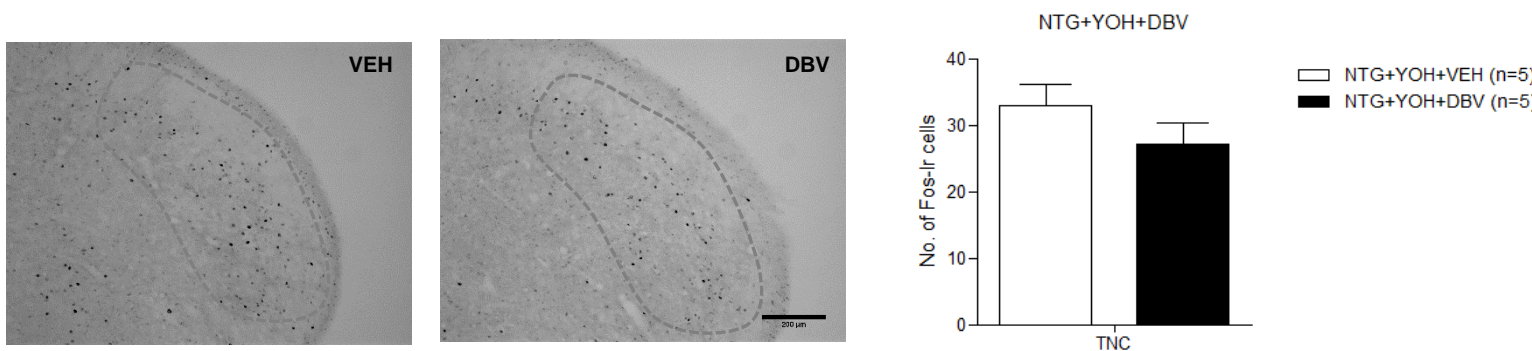
8. Effect of opioid receptor on Feng fu acupoint DBV-treated Fos expression in TNC



9. Involvement of α2 adrenoceptors on DBV treated into Feng fu acupoint effect



10. Effect of α2 adrenoceptors on Feng fu acupoint DBV-treated Fos expression in TNC



CONCLUSION

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.