The development of mirror image pain in a mouse model of inflammatory pain

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The unilateral peripheral injury or inflammation are produced in bilateral hypersensitivity to pain in the ipsilateral and contralateral sides. This phenomenon so called mirror image pain is reported in clinical pain syndromes and in various animal pain models. However, its mechanism is not fully understood. In the present study, we investigated the mechanism of mirror image pain using the complete Freund's adjuvant (CFA)-induced inflammatory pain model and the capsaicin test. Chronic inflammatory pain was induced by injecting CFA into the plantar surface of the left hindpaw and assessed the mechanical allodynia by von Frey filament test. After CFA injection, the paw withdrawal threshold to mechanical stimuli decreased significantly in the ipsilateral paw (CFA injected paw) but not in the contralateral paw (CFA non-injected paw). The decrease in mechanical threshold was observed at 1 day and reached a minimum at 3 days after CFA injection. In saline-treated mice, the mechanical allodynia was not observed. On the other hand, capsaicin is a valuable pharmacological tool for investigating the physiological role of the sensory C-fiber neurons. Capsaicin produced nociceptive behaviors consisting of licking/biting toward the capsaicin-injected paw. Interestingly, in mice pretreated with CFA in the left hindpaw 3 days before, injection of low-dose (this dose did not produce significant pain-related behaviors) capsaicin in the right hindpaw induced the remarkable pain-related behaviors against the left hindpaw (capsaicin non-injected paw). This phenomenon is recognized mirror-image pain, and was dose-dependently attenuated by the administration of TRPV₁ receptor or NMDA receptor antagonist. These results suggest that the mirror image pain observed in CFA-induced inflammatory pain model, is mediated by TRPV₁ or NMDA receptor.