

## News Release

### Title

Conditioned pain modulation: comparison of the effects on nociceptive and non-nociceptive blink reflex

### Key Points

- **CPM was observed objectively using blink reflexes and a cold stimulus to the hand**
- **Nociceptive- but not non-nociceptive blink reflex was suppressed**
- **Perceived sensations were suppressed for both noxious and innocuous stimuli**
- **Effects on the sensation suggested mechanisms higher than the medulla**
- **Results of blink reflex indicated pain-specific mechanisms at medullary dorsal horn**

### Summary

Although conditioned pain modulation (CPM) is considered to represent descending pain inhibitory mechanisms triggered by noxious stimuli applied to a remote area, there have been no previous studies comparing CPM between pain and tactile systems. In this study, we compared CPM between the two systems objectively using blink reflexes. Intra-epidermal electrical stimulation (IES) and transcutaneous electrical stimulation (TS) were applied to the right skin area over the supraorbital foramen to evoke a nociceptive or a non-nociceptive blink reflex, respectively, in 15 healthy males. In the test session, IES or TS were applied six times and subjects reported the intensity of each stimulus on a numerical rating scale (NRS). Blink reflexes were measured using electromyography (R2). The first and second sessions were control sessions, while in the third session, the left hand was immersed in cold water at 10°C as a conditioning stimulus. The magnitude of the R2 blink and NRS scores were compared among the sessions by 2-way ANOVA. Both the NRS score and nociceptive R2 were significantly decreased in the third session for IES, with a significant correlation between the two variables; whereas, TS-induced non-nociceptive R2 did not change among the sessions. Although the conditioning stimulus decreased the NRS score for TS, the CPM effect was significantly smaller than that for IES ( $p = 0.002$ ). The present findings suggest the presence of a pain-specific CPM effect to a heterotopic noxious stimulus.

### Research Background

Conditioned pain modulation (CPM) is a phenomenon in which nociceptive pain is suppressed by noxious stimuli to distant sites. CPM is thought to reflect functions of the endogenous analgesic system, and has been clinically linked to chronic pain and postoperative prolonged pain. Although various methods have been used for measuring CPM, it is difficult to measure CPM objectively in humans. In order to confirm the phenomenon objectively, we conducted a study to evaluate CPM using a method with blink reflex and intraepidermal

electrical stimulation (IES). IES is a selective pain stimulation method that is easy to control. Blink reflexes are an unconscious event and can be an objective indicator.

**Methods:** Fifteen healthy adult volunteers participated in the study. The right forehead was stimulated by IES and blinks were recorded from the orbicularis muscle with electromyograms (EMG). Stimulation was performed 6 times in a session with an interval of 15 s, and EMGs and numerical rating scale (NRS) scores of pain were recorded for each stimulation. Three sessions were repeated that were identical with an exception that the third session was performed with the left (opposite side of the stimulus) hand immersed in 10 ° C cold water. There was a 5-min interval between sessions.

**Analysis:** Each EMG waveform was rectified and averaged in a session. Using the averaged EMG waveforms, the area under the curve (AUC) of the R2 component was calculated. NRS scores were similarly averaged for each session. AUC and NRS values were compared among sessions using one-way ANOVA.

## **Research Results**

Cold water conditioning significantly suppressed both IES-induced subjective pain ( $p = 0.000004$ ) and R2 component ( $p = 0.028$ ). There was a positive correlation between the effect on pain sensations and R2 ( $R = 0.64$ ,  $p = 0.01$ ). On the other hand, the conditioning stimulus showed no effects on TS-induced R2.

## **Research Summary and Future Perspective**

The results supported diffuse noxious inhibitory controls (DNIC) described in rats by Le Bar. For clinical application, comparing the intensity of pain following IES to the forehead between two sessions, with and without conditioning, is considered to be a simple and realistic way to evaluate the endogenous analgesic system.

## **Publication**

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