Mechanisms of pain relief by vibration and movement

Ryusuke Kakigi, Horoshi Shibasaki

Abstract
Mechanisms of pain relief induced by vibration and movement were investigated. A CO₂ laser beam, which is useful for pure nociceptive stimulation, was used for recording pain-related somatosensory evoked potentials (pain SEPs) and for measuring pain threshold and reaction time (RT). Concurrently applied vibratory stimuli to and active movements of the fingers significantly reduced and prolonged pain SEPs, increased pain threshold, and prolonged RT; indicating that an increase in the inhibitory mechanisms of painful feeling was induced by the concurrently adopted sensory inputs mediated by large myelinated fibres. In contrast, continuous cooling enhanced pain SEPs and decreased pain threshold, probably due to the spatial summation of two kinds of nociceptive impulses mediated by the same pathways. The results of this investigation throw light on the mechanisms of the alleviation of pain by vibration and movement.

One of the main hypotheses for the gate control theory reported by Melzack and Wall is that afferent signals which are mediated by large myelinated fibres inhibit small pain fibres presynaptically in the dorsal horn of the spinal cord. This hypothesis is supported by the analgesic effect of transcutaneous electrical nerve stimulation (TENS) of the peripheral nerve. There has been no method of evaluating its effect objectively, and quantitatively, however, owing to the lack of a method of applying pure thermal or painful stimuli while recording the responses from the CNS in humans. Golding et al. and Nardone and Schieppati reported the effects of TENS on waveforms of electrically-stimulated somatosensory evoked potentials (SEPs) for elucidating analgesic effects by TENS, but electric stimuli are not appropriate for the objective described above.

We studied SEPs induced by painful but tolerable CO₂ laser beam (pain SEPs) and proved that ascending sensory signals induced by the beam are mediated by A delta fibres and the spinothalamic or spinoreticular tracts. Pain SEP findings significantly correlate with an impairment of pain-temperature sensation. We analysed the effects of various interference stimuli such as vibration, movement, touch, and cooling on the pain SEPs, pain threshold, and reaction time (RT) to the painful stimuli induced by CO₂ laser stimulation. We aimed to confirm, by using objective methods, the analgesic effect by afferent signals mediated by large fibres and to elucidate its underlying mechanisms.

Subjects and methods
Fifteen normal volunteers, 11 women and four men, were studied. Their ages ranged from 21 to 36 years with the mean age of 25. Their height ranged from 150 to 174 cm (mean 158). No medication was given for sedation, and subjects were kept awake. Each subject gave informed consent. A special CO₂ laser stimulator for recording SEPs was made by Nippon Infrared Industries (Kawasaki, Japan). Its maximum power was 12.5 W, and the stimulus intensity could be continuously changed. The laser wavelength was 10.6 μm, the diameter of the irradiation beam was about 2 mm, and the stimulus duration was 20 msec. We adopted an intensity of approximately 18 mJ/mm² which elicited sharp pain that all subjects described as tolerable, “like a pin-prick”. To avoid habituation irradiated points were moved slightly for each stimulus. The laser beam was applied to the part of the dorsum of hand innervated by the radial nerve once every 3 seconds. Subjects’ eyes were protected by swimming goggles.

Silver disc electrodes (1 cm diameter) were attached to the scalp with collodion and filled with electrode jelly based on the international 10–20 system. An impedance was maintained at less than 3 kΩ. Three exploring electrodes were placed at Cz, C1, and C2 (2 cm behind Cz, and C1, respectively). The latter two sites corresponded to the hand sensory area of each hemisphere. Linked ear lobes (A1 ± A2) were used as the reference. The amplifier frequency response was 0.5–30 Hz (−3dB). The analysis time was 1 second, and the sampling rate was 1.97 ms. Peak latency and amplitude were measured for each recognisable component by a computer cursor. Amplitude was measured from the preceding peak of the opposite polarity. Relative positivity at grid 1 resulted in a downward deflection. Interfering stimuli were continuously applied to the fingers of the same hand throughout each recording session of pain SEPs as follows. (1) Tactile stimulation: the dorsum of the 2nd and 3rd fingers was continuously stroked by the experimenter with a soft wad of tissue paper. (2) Vibration: vibratory stimulus with a frequency of approximately 500 Hz was applied to the dorsum of the 2nd and 3rd fingers with a battery powered...
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applied the skin, subjects were requested to tell the examiner when they began feeling distinct sharp pain "like a pinprick". The test was repeated at least three times and the lowest threshold was adopted. Reaction time (RT) to the CO2 laser beam was measured in the "control" and each "interference" condition. Stimulus intensity was the same as that employed for recording pain SEPs. An interstimulus interval was at random and 3 seconds or longer. The subject was required to push a button as soon as the painful sensation was felt. More than 10 RTs were measured for each condition and the mean calculated. For comparison, RT to the electrical stimulus delivered to the median nerve at the wrist was also measured by the same paradigm as used for CO2 laser stimulation. The electrical stimulus was a constant voltage square-wave pulse lasting 0-2 ms, and its stimulus intensity was sufficient to produce a definite twitch of the thumb. Statistical analysis of pain SEP findings, pain threshold, and RT was done by paired t test between the "control" and each "interference" condition, and p < 0-02 was accepted as significant.

Results

PAIN SEP FINDINGS

A small negative and a large positive potential, termed N1 and P1, respectively, were identified in the "control" and each "interference" trial in all 15 subjects. As the responses recorded at the Cz electrode were much larger than those at C3 or C4 (figure 1) the former were analysed. The mean peak latencies of N1 and P1 in the "control" were 204-6 and 302-5 ms, respectively, and their amplitudes were 2-23 μV and 0-07 μV, respectively (table 1). Amplitude of both N1 and P1 recorded at C4 was not significantly different from that at C3.

Peak latencies of N1 and P1 were significantly prolonged in "movement" and "vibration" interference (table 1 and figure 2). Amplitude of both N1 and P1 was decreased by "movement" and "vibration" interference, and a change of P1 in both conditions was significantly large (p < 0-01; table 1 and figure 2). Amplitude change by "tactile" interference was not consistent. In contrast, amplitude of both N1 and P1 was increased by the "cooling" interference, particularly P1 (p < 0-01; table 1 and figure 2). Wave form changes were also identified in each interference condition recorded at the C3, C4, and Cz electrode, but their degrees were much smaller than those at the Cz. For example, the percentage of the amplitude decreased by the "movement" interference was 18-9%, 40-3%, and 20-0% at the C3, C4, Cz, and C4 electrode, respectively.

PAIN THRESHOLD

The mean (SD) of pain threshold in "control" was 13-6 (0-5) mJ/mm2. Pain thresholds in "movement" and "vibration" interference conditions were the same with or higher than that of "control" in all subjects, and their changes were significant, particularly for "vibration" interference (table 2). In contrast, pain threshold in the "cooling" interference condition was the same as or smaller than that of "control" in all subjects, and the difference between them was significant (table 2).

REACTION TIME (RT)

The mean (SD) RT to the CO2 laser stimulus in the "control" condition was 334-7 (27-2) ms. It was increased in all "interference" conditions except "cooling", and the change in "movement" and "vibration" interference was significant (table 3). The mean (SD) RT to electrical stimulation applied to the median nerve at the wrist was 170-0 (30-2) ms. The difference between the peak latency of N1 and RT (N1-RT) was also measured; that in "movement" and "vibration" interference conditions was significantly longer than that in the "control" condition (table 3). N1-RT in the "tactile" and "cooling" interference conditions was shorter than that in the "control" condition, but the changes were not significant. As the peak latency of P1 was longer than RT in several subjects, P1-RT was not measured.

Figure 1 Averaged wave forms of pain SEPs recorded at C3, C4, and Cz electrode after CO2 laser stimulation to left hand with no interference (control wave form) in normal subject. Linked ear lobes were used as reference. Traces on top are superimposition of eight recordings at Cz electrode.
Table 1  Latencies and amplitudes of pain SEPs recorded at Cz without (control) and with various interference

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Tactile</th>
<th>Movement</th>
<th>Vibration</th>
<th>Cooling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
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<tr>
<td>peak latency (msec)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>205 ± 4</td>
<td>216 ± 3</td>
<td>232 ± 2</td>
<td>232 ± 2</td>
<td>278 ± 4</td>
</tr>
<tr>
<td>P1</td>
<td>302 ± 4</td>
<td>310 ± 4</td>
<td>317 ± 4</td>
<td>317 ± 4</td>
<td>312 ± 4</td>
</tr>
<tr>
<td>Mean (SD) amplitude (uV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>2.2 ± 0.2</td>
<td>3.2 ± 0.3</td>
<td>1.8 ± 0.2</td>
<td>1.8 ± 0.2</td>
<td>4.8 ± 0.3</td>
</tr>
<tr>
<td>P1</td>
<td>8.0 ± 2.7</td>
<td>9.1 ± 4.0</td>
<td>6.8 ± 2.7</td>
<td>6.8 ± 2.7</td>
<td>10.5 ± 4.5</td>
</tr>
</tbody>
</table>

Significance of difference between control and each interference trial calculated by paired t test (*p < 0.05, **p < 0.01).
Mechanisms underlying an particular phenomenon might have the effects of pain SEP by "movement", "vibration", or "tactile" interference, which are generally explained by this hypothesis. In addition, we propose two hypotheses in relation to the cognitive process as a higher function of the CNS. The first is that humans cannot completely differentiate painful stimulation from sensory stimulation of other modalities which are applied concurrently, and tend to neglect unpleasant sensations. The second is that painful sensation is attenuated by an attention to ascending signals of other modalities such as vibration.

The effects of "tactile" interference were fairly small compared with those of active movement or vibration interference, suggesting that the signals mediated by small fibres are not attenuated as much as those mediated by cutaneous sensory fibres as by movement or vibration. A prominent "tactile" interference effect on electric SEPs has to be explained by a different mechanism underlying the interference between them. It is difficult to elucidate the underlying mechanisms of the contrary effect by the cooling interference. Continuous stimulation of the nociceptors by cooling during the superimposed laser stimulation might increase the excitability of the appropriate dorsal horn neurons and then that particular phenomenon might have the effects of increasing the synchronicity of the volley and the number of spinothalamic tract fibres producing an increased amplitude of N1 and P1 and a reduction of the pain threshold. The fact that painful sensation caused by injury in cold weather is felt more than that in warm weather might be compatible with this particular finding.

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Table 2: Pain threshold (mV/mm²) in "control" and each "interference" condition

<table>
<thead>
<tr>
<th>Condition</th>
<th>Control</th>
<th>Tactile</th>
<th>Movement</th>
<th>Vibration</th>
<th>Cooling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>13.6 (0.5)</td>
<td>13.9 (0.6)</td>
<td>14.5** (0.5)</td>
<td>14.9 (0.5)</td>
<td>13.1** (0.4)</td>
</tr>
</tbody>
</table>

Significance of difference between control and each interference trial calculated by paired t test (*p < 0.02, **p < 0.01).

Table 3: Reaction time (RT) (ms) to CO2 laser stimulation and the time interval between N1 of pain SEP and RT in "control" and each "interference" condition

<table>
<thead>
<tr>
<th>Condition</th>
<th>Control</th>
<th>Tactile</th>
<th>Movement</th>
<th>Vibration</th>
<th>Cooling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>334.7 (27.2)</td>
<td>341.6 (29.8)</td>
<td>372.0** (37.7)</td>
<td>398.7** (57.3)</td>
<td>323.0 (33.4)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>129.1 (30.2)</td>
<td>124.8 (41.2)</td>
<td>147.6* (30.5)</td>
<td>166.7** (58.7)</td>
<td>111.7 (25.7)</td>
</tr>
</tbody>
</table>

Significance of difference between control and each interference trial calculated by paired t test (*p < 0.02, **p < 0.01).


