Inhibitory Effect of Pain-Eliciting Transcutaneous Electrical Stimulation on Vibration-Induced Finger Flexion Reflex in the Human Upper Limb

N. TAKAKURA*,†,‡, H. YAJIMA*,†, and I. HOMMA†,‡

*Hanada College: Japan School of Acupuncture, Moxibustion and Physiotherapy, 20-1 Sakuragaoka-machi, Shibuya-ku, Tokyo, 150-0031 Japan; †Institute of Foundation for Oriental Medicine Research, 28-9 Sakuragaoka-machi, Shibuya-ku, Tokyo, 150-0031 Japan; and ‡Second Department of Physiology, Showa University School of Medicine, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo, 142-8555 Japan

Abstract: We studied the effects of non-pain transcutaneous electrical stimulation (TES) and pain-eliciting TES on vibration-induced finger flexion reflex (VFR) in 12 healthy volunteers. Tonic finger flexion reflex in the upper limb was induced by the application of vibratory stimulation on the volar side of the middle fingertip in the right hand before and after TES. Non-pain TES or pain-eliciting TES was applied on the skin between the bases of the first and second metacarpals in the right hand dorsal area in a crossover design. Pain-eliciting TES inhibited VFRs significantly (Fisher’s PLSD, \( p < 0.01 \)), compared to those of the time-control group during and after TES. VFRs were reduced approximately to 63.8% and 78.6% of prestimulation flexion force during and after pain-eliciting TES, respectively. Nonpain TES did not inhibit VFR. These results suggest that pain-conducting afferent fibers have inhibitory neuronal connection over the ipsilateral reflex circuits of VFR in the upper limb. [The Japanese Journal of Physiology 54: 243–248, 2004]

Key words: vibration, flexion reflex, electrical stimulation, noxious stimulation, acupuncture.

Vibration on the volar side of the fingertip elicits a tonic flexion reflex in the vibrated finger [1]. This reflex is called vibration-induced finger flexion reflex (VFR) [1]. The vibrating finger goes into flexion when the start of vibration and finger flexion force gradually increases during vibration [1]. Such VFR disappears immediately after the cessation of vibratory stimulation. This reflex is inferred to have two reflex arcs from the cross correlogram between vibratory stimuli and motor unit spikes in the flexion muscle: the spinal short loop and the supraspinal long loop [2, 3]. The receptor of this reflex is assumed to be the skin mechanoreceptor because VFR is markedly reduced when the fingertip is anesthetized or cooled [1, 4–6].

We previously reported the inhibitory effects of noxious mechanical stimulation of a needle insertion, namely acupuncture, in the upper limb on VFR [3, 7–9]. Needle penetration is a noxious stimulus [10]. For that reason, we inferred that activities in small or medium-sized pain-conducting afferent fibers may participate importantly in VFR inhibition. In fact, the inhibitory effects induced by needle insertion with the manipulation giving stronger stimulation are remarkably stronger than those by needle insertion with manipulation giving less stimulation [8]. Current assumptions for afferent fiber participation in inducing efficacies by fine needle insertion are small or medium-sized fibers [10]. These results suggest that, in the upper limb, small or medium-sized pain-conducting afferent fibers have an inhibitory connection to the reflex circuits of VFR.

The effects of transcutaneous electrical stimulation (TES) on motoneuronal activities have been investigated extensively in humans [11–15]. Those studies show that the inhibitory effects of high-intensity noxious TES on motoneuronal excitability in the upper...
limb [11, 12, 13] and the inhibitory effects of the lower limb flexor motoneurons by low-intensity nonnoxious TES [14, 15]. Further tonic vibration reflex in the extensor carpi radialis muscle is inhibited by innocuous cutaneous stimulation applied to the dorsal side of the forearm [16]. These results suggest the possibility of a contribution of low threshold large-diameter afferent fibers in producing VFR inhibition by acupuncture.

Therefore this study is intended to elucidate whether nonpain TES or pain-eliciting TES to the dorsal hand inhibit ipsilateral VFR in the upper limb. Thereby, we can determine the necessity of noxious characteristics of somato-sensory stimulation in inhibitory action over VFR in the upper limb.

METHODS

The Ethics Committee of Showa University approved this study. Twelve healthy volunteers (mean ± SD age 26 ± 5 years, 9 males, 3 females) participated as subjects. This experiment has a crossover design with time-control, nonpain TES, and pain-eliciting TES. All subjects gave written informed consent after the purpose and format of this study were explained to them. Each experiment was performed at about the same time on different days.

Figure 1 shows the experimental setting. A subject was seated in a chair, the position of which was adjustable. The right forearm of a subject was placed on a pad to ensure that a consistent position was maintained from one experiment to another. The forearm was immobilized, leaving the finger joints free and maintaining the hand in a prone-position and extended at an angle of approximately 30°. The wrist and elbow joint movements were restricted. The volar side of the right middle fingertip was placed on a pressure transducer attached to a vibrator. Thereafter subjects pressed the pressure transducer slightly as a background contraction. When the background contraction was stable, 60 Hz vibration with 1 mm displacement amplitude was applied for 20 s to the volar side of the middle fingertip. Vibration was delivered use of an electromagnetic vibrator (FF 225N; Foster Electric Co., Ltd.) driven by a sine-pulse generator (VP-7421A Function Generator; Matsushita Electrical Industrial Co., Ltd.) coupled to a power amplifier (1076; Bose Corp.). Vibrator amplitude was monitored by a digital oscilloscope (Tectronix TDS 360P; Sony Corp.) to measure the vibrator driving force. The driving force of the vibrator was 3.5–4.0 V. The subjects were blindfolded throughout the trial. Tonic finger flexion force induced by vibration was measured isometrically with a force transducer (9E01-L2-5K; NEC San-ei Instruments, Ltd.) placed between an attachment of the vibrator and the fingertip, through an amplifier (6M67; NEC San-ei Instruments, Ltd.). Force measurements were then recorded with a pen recorder (VP-6712A; Matsushita communication Industrial Co., Ltd.). Respective flexion forces of VFRs were measured before, during, and after TES.

We used electrical stimulation to elicit pain because the electrical stimulation at the pain threshold, the point at which a subject perceives pain, surely activates pain-conducting afferent fibers [17, 18]. One surface electrode was placed at approximately the midpoint of the radial side of the second metacarpal; another one was placed between the two heads of the first and second metacarpals in the right-hand dorsal area to deliver TES. The surface electrode at the proximal point was connected to the negative clip, and the positive clip was connected to the surface electrode on the distal point. Electrical stimuli were delivered with a constant-voltage isolation unit (SEN-3301, SS-104J; Nihon Kohden Corp.) via two surface electrodes with a maximal output of 200 V. The stimulator was set to deliver square wave pulse trains of 0.1 ms duration at 1 s intervals. Prior to the experiment, we determined what strengths of stimulation (square wave pulse: duration, 0.1 ms; interval, 1 s) constituted the perception and pain thresholds for individual subjects. Mean ± SD intensity for the nonpain TES group was 24.6 ± 12.6 V; and that of the pain-eliciting TES group was 74.5 ± 18.7 V. We delivered electrical stimulation at the perception threshold (nonpain TES) that subjects felt tactile sensation clearly or at the pain threshold (pain-eliciting TES) that subjects felt pain clearly for 5 min. Flexion forces were measured at 10 min (before 1) and 5 min before (before 2) electrical stimulation,
Inhibitory Effect of Pain-Eliciting Transcutaneous Electrical Stimulation

We studied the inhibitory effects of nonpainful or pain-eliciting cutaneous electrical stimulation on tonically activated flexion reflex in the upper limbs evoked by nonnoxious mechanical stimulation. Pain-eliciting electrical stimulation applied to the skin covering the dorsal side of the hand innervated with the radial nerve produced a prominent decrease in VFR during and after electrical stimulation. In contrast, VFR during and after nonpain stimulation did not decrease in any subjects. Figure 2 shows traces of finger flexion force induced by VFR in a typical subject before, during, and after TES. In this subject, VFR decreased after pain-eliciting TES, but VFR after nonpain TES did not. Compared to prestimulation values (1.13 N), maximum flexion force during 1 and after pain-eliciting TES (after 1) decreased 1.13 N (58.0%) and 0.72 N (36.9%), respectively; and those after nonpain TES were 0.17 N (8.9%) and 0.09 N (4.7%), respectively. For these 12 subjects, the overall mean ± SD (N) decreases in maximum flexion force for the pain-eliciting stimulation group (during 1, 0.65 ± 0.55; after 1, 0.81 ± 1.32) were significantly larger (p < 0.01) than those of the time-control group (during 1, –0.23 ± 0.56; after 1, –0.26 ± 0.58) and nonpainful stimulation group (during 1, –0.22 ± 0.46; after 1, –0.09 ± 0.68) (during 1, F(2, 33) = 11.01 p < 0.01; after 1, F(2, 33) = 4.69 p < 0.05). Nevertheless, mean ± SD (N) decrease in maximum flexion force for the pain-eliciting TES group before 2 was not significantly larger (p > 0.05) than that of the time-control group and nonpainful TES group (F(2, 33) = 1.21 p = 0.31).

Table 1 shows summary results (mean ± SD%) for data recorded from 12 subjects. Mean maximum flexion forces for the pain-eliciting TES group were decreased
Table 1. Mean [SD] % of Before 1 of maximum flexion force (left columns) and AUC (area of under curve of flexion force; right columns).

<table>
<thead>
<tr>
<th>Time-control</th>
<th>Pain-eliciting TES</th>
<th>Non-pain TES</th>
<th>F (2, 33) and P value</th>
<th>AUC</th>
<th>Time-control</th>
<th>Pain-eliciting TES</th>
<th>Non-pain TES</th>
<th>F (2, 33) and P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>During 1</td>
<td>109.0 [22.8]</td>
<td><strong>71.7 [26.5]</strong></td>
<td>108.9 [29.5]</td>
<td>F = 7.92, P = 0.002</td>
<td>106.9 [19.1]</td>
<td><em>69.5 [31.2]</em>*</td>
<td>108.4 [32.7]</td>
<td>F = 7.29, P = 0.002</td>
</tr>
<tr>
<td>During 2</td>
<td>111.6 [20.3]</td>
<td><strong>55.8 [28.5]</strong></td>
<td>110.7 [31.7]</td>
<td>F = 16.53, P &lt; 0.0001</td>
<td>110.0 [21.1]</td>
<td><em>55.8 [29.3]</em>*</td>
<td>102.5 [32.5]</td>
<td>F = 13.16, P &lt; 0.0001</td>
</tr>
<tr>
<td>After 1</td>
<td>120.2 [26.7]</td>
<td><strong>68.0 [35.8]</strong></td>
<td>104.8 [33.1]</td>
<td>F = 6.49, P = 0.004</td>
<td>105.9 [29.3]</td>
<td><strong>67.0 [30.8]</strong></td>
<td>92.2 [25.8]</td>
<td>F = 6.65, P = 0.004</td>
</tr>
<tr>
<td>After 2</td>
<td>107.9 [14.9]</td>
<td>*82.1 [37.2]</td>
<td>101.8 [25.8]</td>
<td>F = 2.99, P = 0.070</td>
<td>108.4 [16.0]</td>
<td><em>81.9 [32.7]</em>*</td>
<td>108.1 [28.0]</td>
<td>F = 3.93, P = 0.030</td>
</tr>
<tr>
<td>After 3</td>
<td>101.2 [15.8]</td>
<td>85.7 [31.9]</td>
<td>111.8 [37.4]</td>
<td>F = 2.34, P = 0.112</td>
<td>102.9 [21.9]</td>
<td><em>83.2 [22.1]</em>*</td>
<td>106.9 [24.8]</td>
<td>F = 3.66, P = 0.037</td>
</tr>
</tbody>
</table>

Note 1: * (P < 0.05) or ** (P < 0.01) indicates mean % was significantly different from that of time-control in the same row for maximum flexion force and AUC, respectively.

Note 2: ¶ (P < 0.05) or ¶¶ (P < 0.01) indicates mean % was significantly different from that of non-pain TES in the same row for maximum flexion force and AUC, respectively. Note 3: Before 1, 10 min before TES; Before 2, 5 min before TES; During 1, immediately after onset of TES; During 2, 4.5 min after onset of TES; After 1, immediately after TES; After 2, 5 min after TES; After 3, 10 min after TES.

In a healthy human, an application of vibratory stimulation on the volar side of the fingertip induces a flexion reflex; typically, finger flexion force occurs with the onset of vibration and increases progressively during vibration [14, 19]. Several lines of study show that the maximum flexion force is reliable as an index of this reflex [2–5, 19].

**DISCUSSION**

The mean maximum flexion force for the pain-eliciting TES group was significantly lower than that of the time-control group from during 1 to after 1. The mean maximum flexion force for the non-pain TES group was not significantly lower compared to that of the time-control group.

Besides maximum flexion force, we measured the AUC of flexion force to confirm the credibility of maximum flexion force during VFR as the index of this reflex [2–5, 19]. The mean percentages in the maximum flexion forces were quite similar to those in the AUC in Table 1. The mean AUCs for the pain-eliciting TES group were significantly lower than those of the time-control group from during 1 to after 3. The mean AUCs in the non-pain TES group were not significantly lower compared to those of the time-control group. Moreoever, we tested for correlation of maximum flexion force and AUC. Significant positive correlation (r = 0.83, P < 0.01) was revealed between maximum flexion force and AUC (Fig. 3). These results suggest that maximum flexion force, used as an indication of VFR in the previous studies, is credible [2–5, 7–9, 19].

**Fig. 3.** Correlation between maximum flexion force and AUC.

Significant positive correlation between maximum flexion force and AUC (r = 0.83, P = 0.01).
Inhibitory Effect of Pain-Eliciting Transcutaneous Electrical Stimulation

This innocuous-stimulation-induced flexion reflex is inhibited by acupuncture with needle penetration [7–9, 20–24]. Furthermore, when stimulation intensity by acupuncture is greater, the inhibitory effect over VFR is also greater [8]. We infer that the noxious characteristic of the somato-sensory stimulation is the key factor giving rise to VFR inhibition because needle penetration is noxious stimulation with tissue injury, which may activate small and medium-sized pain-conducting afferent fibers [10]. However, the possibility of the contribution of low threshold large-diameter afferent fibers [16, 25] in producing VFR inhibition is not out of the question. We studied the inhibitory effect on VFR by pain-eliciting TES, which activates pain-conducting afferent fibers [17, 18], and nonpain TES to clarify whether VFR inhibition required activities of pain-conducting afferent fibers. The present study showed that pain-eliciting TES inhibited VFR, but nonpain TES did not. These results suggest that the noxious component of afferent activities was necessary to produce VFR inhibition in the upper limb. Therefore we reasoned that an inhibitory neural connection exists from the pain-conducting afferent fibers to the VFR circuits.

It is an extremely interesting issue whether inhibitory action by afferent activities occurs at terminals of the primary afferent or at the motoneuronal level in VFR neural circuits. Alterations in motoneuronal excitability induced by cutaneous afferent stimulation have been studied by electromyographic recordings. During isometric voluntary contraction of upper-limb muscles, a single painful electrical stimulation restricted to cutaneous nerves in the finger engenders a suppression of EMG activity (silent period, SP) [11, 13]. Further, high-intensity finger stimulation suppressed H-reflexes and F-waves; they occur during the time corresponding to the SP [12, 13]. These studies suggest that spinal motoneurons are inhibited by activities from nociceptive stimulation on cutaneous noxious afferent fibers. Moreover, animal experiments have implied that nociceptive afferent activity has inhibitory and facilitatory effects on FRA-evoked EPSPs in α-motoneurons [26, 27]. These effects result from a convergence between nociceptive and nonnociceptive afferents of different origin onto common interneurons in segment reflex pathways to α-motoneurons [26, 27]. We consider that sensory perception in the finger does not change by electrical stimulation to the forearm [28]. For that reason, we infer that VFR inhibition might be produced by noxious somatosensory input on the motoneurons innervated to the flexor muscles via common interneurons by which the motoneurons are facilitated by vibration in the spinal cord [21], but not those afferents innervated to the finger.

Along with pain-eliciting TES, VFR inhibition was observed not only during needle insertion, but also subsequently [3, 7–9, 20–23]. This characteristic of inhibition implies that acupuncture inhibits motoneuronal activities of VFR reflex circuits just as pain-eliciting TES does. A high intensity of somato-sensory input to evoke excitation in noxious afferents, e.g., pain-eliciting transcutaneous electrical nerve stimulation, might be a potential complimentary treatment of spasticity, especially in upper limbs because the overall excitability of motoneurons in spastic patients is reducible by noxious high-intensity stimulation [11–13, 28]. Patients suffer pain or discomfort during TES at high-intensity to reduce motoneuronal activities [28]. In contrast to painful TES, acupuncture with a fine needle elicits little pain during insertion despite the activation of noxious afferent fibers [10]. Therefore acupuncture, rather than high-intensity TES, is recommended for reducing muscle spasticity.

In conclusion, pain-eliciting electrical stimulation to the skin in the dorsal hand inhibited VFR, but nonpain stimulation did not. We conclude that pain-conducting afferent fibers have inhibitory connection to the ipsilateral reflex circuits of VFR in the upper limb.

We thank Dr. Takemasa Shiraishi (Institute of Foundation for Oriental Medicine Research, Tokyo) for reviewing this manuscript.

REFERENCES

8. Takakura N, Ogawa H, Iijima S, Nishimura K, Kanamaru A, Sibuya M, and Homma I: Effect of acupuncture at...