Afferent nerve fibers and acupuncture

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Abstract

Acupuncture has been used for analgesia, for treating visceral function disorders and for improving motor functions. It is well established that stimulation of the skin and muscles, either electrically or with noxious or non-noxious stimuli, induces a variety of somato-motor and autonomic responses. This strongly suggests that acupuncture acts by exciting cutaneous and/or muscular afferent nerve fibers. A question of considerable scientific and practical interest is what kinds of somatic afferent fibers are stimulated by acupuncture and are involved in its effects. There are several types of afferent fiber: thick myelinated Aα and Aβ (group I and II), thin myelinated Aδ (group III) and thinner unmyelinated C (group IV) fibers. In recent studies we have tried to establish which ones of these types of somatic afferent fiber are stimulated by acupuncture. In this article we first review the experimental evidence showing that the effects of acupuncture are mediated by the activation of afferent nerve fibers innervating the skin and muscles. Secondly, we discuss what types of afferent nerve fiber are activated by electrical acupuncture, and what types are involved in its effects on somato-motor functions and on visceral functions. Finally, we present some new findings based on recordings from single afferent nerve fibers excited by manual acupuncture.

Keywords: Afferent nerves, Acupuncture, Visceral functions, Motor functions

1. Introduction

Acupuncture has been used clinically to induce different forms of analgesia in addition to adjustment of visceral functions (Mann, 1987; Stux and Pomeranz, 1998). The primary mechanism whereby acupuncture elicits these clinical effects appears to be through the activation of afferent nerve fibers innervating the skin and muscles by acupuncture needle stimulation (Sato et al., 1994, 1997; Stux and Pomeranz, 1998). Somatic afferent nerve fibers are composed of groups I, II, III and IV fibers (or Aα, β, δ and C-fibers, respectively). Acupuncture stimulation has been reported to excite various afferent fiber groups. The somatic afferent information of nerve fibers excited by acupuncture stimulation has various effects on body function, including an inhibitory effect on the synaptic transmission of nociceptive inputs in the central nervous system (CNS), resulting in analgesia or suppression of pain, and production of various reflex responses, including somatic, autonomic, and hormonal responses.

In this article we first review the experimental evidence showing that the effects of acupuncture are mediated by the activation of afferent nerve fibers innervating the skin and muscles. Secondly, we discuss what types of afferent nerve fiber are activated by electrical acupuncture, and what types are involved in its effects on somato-motor functions and on visceral functions. Finally, we present some new findings based on recordings from single afferent nerve fibers excited by manual acupuncture.

2. Regulation of visceral functions (somato-autonomic reflex)

Acupuncture has been used to improve the disturbances of visceral autonomic functions (Mann, 1987; Li and Yao, 1992; Stux and Pomeranz, 1998). Recent acupuncture studies in anesthetized animals demonstrated that acupuncture-like stimulation in various areas produced reflex responses of various visceral functions. These acupuncture-like stimulation-induced responses have been proven to be reflexes in which afferents are cutaneous and muscle somatic afferent nerves, and efferents are autonomic efferent nerves.

2.1. Manual acupuncture

2.1.1. Hindleg

Manual acupuncture-like stimulation of a hindleg has been reported to modify gastric motility, blood pressure, heart rate and the secretion rates of adrenal medullary catecholamine hormones (adrenaline and noradrenaline) using anesthetized rats (Sato et al., 1993, 1996; Ohsawa et al., 1995; Kobayashi et al., 1998; Uchida et al., 2007; 2008) (Table 1).

These acupuncture effects were eliminated after the somatic afferent nerves (femoral nerve and sciatic nerve) innervating the
needle insertion site were surgically severed. The acupuncture-like stimulation increased the somatic afferent nerve activity recorded from the nerve branches innervating the stimulation site. These findings indicate that the effects of the acupuncture-like stimulation on visceral function were elicited when the action potential of the afferent nerves was delivered to the central nervous system.

2.1.1. Skin and muscle. Gastric motility was excited when a hindpaw was stimulated, in all cases in which stimulus was delivered to the skin and muscles, the skin only, and underlying muscles alone. These responses following stimulation of either the hindpaw skin or the underlying muscles tended to be smaller than the response evoked by stimulating the skin and muscles together (Sato et al., 1993).

Stimulation of the skin alone had no significant effect on mean arterial blood pressure (MAP) or heart rate (HR). On the contrary, stimulation of the muscles alone produced significant and remarkable decreases in MAP and HR (Ohsawa et al., 1995; Uchida et al., 2007).

2.1.1.2. Needle diameter. In the response of HR and gastric motility, the difference in the effect caused by the thickness of the acupuncture needle has been examined (Sato et al., 1993; Uchida et al., 2007). The HR and gastric motility response elicited by stimulation with a 340 µm needle were greater than that elicited with a 160 µm needle. This difference may indicate that the HR and gastric motility are affected by a greater amount of somatic afferent excitation since a thick acupuncture needle may excite more afferent nerve fibers than a thin one.

2.1.2. Perineal area

Acupuncture-like stimulation applied to the perineal area inhibited rhythmic micturition contractions (RMCs) (Sato et al., 1992) (Fig. 1B). By contrast, stimulation applied to other areas was ineffective. Stimulation of the perineal skin or underlying muscles, or recorded from the pelvic nerve branches innervating the perineal muscles (Fig. 1A). The stimulation-induced inhibition of RMCs was abolished after surgically severing these nerves. These findings indicate that the inhibition of the RMCs following acupuncture-like stimulation occurs via the activation of afferent nerve when action potentials are delivered to the central nervous system.

2.1.2.1. Skin and muscle. The effects of stimulation applied to either the perineal skin or underlying muscles alone on the RMCs were tested. Either stimulation was effectively inhibited the RMCs; however, stimulation of the muscles produced a stronger inhibition than stimulation of the skin.

2.1.2.2. Needle diameter. The inhibitory effect of a 160 µm needle on the RMCs was similar to that of a 340 µm needle. This may indicate that bladder function is affected by a small amount of somatic afferent excitation compared to the cardiovascular function mentioned above.

2.1.3. Abdomen

Manual acupuncture-like stimulation of the abdomen induced inhibitory gastric responses and the secretion of catecholamines in anesthetized rats (Sato et al., 1993, 1996). The stimulation of the abdomen increased the activity of the spinal afferent nerves ipsilateral to the stimulated site at the T9, T10, T11 and T12 levels. The responses of gastric motility and secretion of catecholamines disappeared after the spinal nerves ipsilateral to the stimulated site between the T8 and T13 levels had been severed.

2.1.3.1. Skin and muscle. Stimulating either the abdominal skin or the underlying muscles alone evoked responses of gastric motility and catecholamine secretion, although the response tended to be less than that elicited by stimulating the skin and muscles together (Sato et al., 1993, 1996).

2.1.4. Forepaw

Stimulation of the forepaw produced increases in cerebral blood flow (CBF) and MAP in spinal cord-intact rats (Uchida et al., 2000) (Fig. 2A, C). After spinal transaction at the first to second thoracic level, the blood pressure response to manual acupuncture stimulation of the forepaw was suppressed, whereas an increase in CBF still occurred. The increase in CBF induced by forepaw stimulation was abolished by severing the somatic nerves at the brachial plexus (Fig. 2C). Forepaw stimulation enhanced the activity of the radial, ulnar, and median nerves (Fig. 2B).

2.2. Electro-acupuncture

The effects of electro-acupuncture (EA) stimulation on several visceral functions were studied using anesthetized rats (Table 1). EA stimulation applied to hindleg induced stimulus intensity-dependent pupil dilation (Fig. 3C), an increase in muscle blood flow (MBF), a decrease in renal blood flow, and response of the catecholamine secretion rate from the adrenal gland (Ohsawa et al., 1997; Noguchi et al., 1999a; 1999b; Mori et al., 2000) (Table 1). EA stimulation applied to the forepaw induced an increase in CBF (Uchida et al., 2000).

Table 1

<table>
<thead>
<tr>
<th>Stimulation site</th>
<th>Afferent</th>
<th>Response</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdomen</td>
<td>TR–T13 spinal n.</td>
<td>Gastric motility ↓</td>
<td>Sato et al. (1993)</td>
</tr>
<tr>
<td>Hindlimb (Zusanli)</td>
<td>Femoral n. and sciatic n.</td>
<td>Gastric motility ↑</td>
<td>Ohsawa et al. (1995)</td>
</tr>
<tr>
<td>Abdomen</td>
<td>TR–T13 spinal n.</td>
<td>Mean arterial pressure ↓</td>
<td>Sato et al. (1996)</td>
</tr>
<tr>
<td>Hindlimb</td>
<td>Sciatic n.</td>
<td>Secretion rates of adrenal medullary catecholamine hormones ↓ or ↑</td>
<td>Sato et al. (1999)</td>
</tr>
<tr>
<td>Hindlimb (Zusanli)</td>
<td>Femoral n. and sciatic n.</td>
<td>Heart rate ↓</td>
<td>Kobayashi et al. (1998)</td>
</tr>
<tr>
<td>Forepaw</td>
<td>Radial n., ulnar n. and median n.</td>
<td>Cortical cerebral blood flow ↑</td>
<td>Uchida et al. (2000)</td>
</tr>
<tr>
<td>Hindlimb (Zusanli)</td>
<td>Femoral n. and sciatic n.</td>
<td>Heart rate ↓</td>
<td>Uchida et al. (2007)</td>
</tr>
<tr>
<td>Electro-acupuncture</td>
<td>Hindpaw</td>
<td>II, III, IV</td>
<td>Pupil diameter ↑</td>
</tr>
<tr>
<td>Hindpaw</td>
<td>III, IV</td>
<td>Blood flow in the muscle biceps femoris ↑ or renal blood flow ↓</td>
<td>Noguchi et al. (1999a)</td>
</tr>
<tr>
<td>Hindpaw</td>
<td>III, IV</td>
<td>Blood flow in the muscle biceps femoris ↓</td>
<td>Noguchi et al. (1999b)</td>
</tr>
<tr>
<td>Hindpaw (Chongyang)</td>
<td>III, IV</td>
<td>Secretion rates of adrenal medullary catecholamine hormones ↑</td>
<td>Mori et al. (2000)</td>
</tr>
<tr>
<td>Hindlimb (Zusanli)</td>
<td>III, IV</td>
<td>Secretion rates of adrenal medullary catecholamine hormones ↓ or ↑</td>
<td>Sato et al. (1999)</td>
</tr>
<tr>
<td>Forepaw</td>
<td>III, IV</td>
<td>Cortical cerebral blood flow ↑</td>
<td>Uchida et al. (2000)</td>
</tr>
</tbody>
</table>

↑: increase, ↓: decrease, →: no change.
It has been demonstrated which populations of afferent nerve fibers are necessary for each response induced by EA stimulation, using selective electrical stimulation of different groups of fibers by altering the intensity of the electrical stimulus and recording the volleys of nerves with different conduction velocities.

2.2.1. Group I afferent fibers

EA stimulation of hindpaw, hindlimb, or forepaw, with stimulus strength sufficient to excite the group I somatic afferent fibers produced no effect on pupil dilation, muscle blood flow, renal blood flow, catecholamine secretion rate from the adrenal gland, and CBF.

Fig. 1. Effect on rhythmic micturition contractions (RMCs) of acupuncture-like manual stimulation in anesthetized rat. A: Effects on the afferent discharges of pudendal or pelvic nerve branches coming from the perineal skin or underlying muscles following acupuncture-like stimulation of the perineal area. B: Effects of the RMCs (at the upper trace), vesical pelvic efferent nerve activity (at the middle trace) and hypogastric efferent nerve activity (at the bottom trace) following acupuncture-like stimulation of the perineal area (modified from Sato et al., 1992).

Fig. 2. The effect of acupuncture-like manual stimulation of forepaw on cortical cerebral blood flow (CBF) in anesthetized rats. A: Schematic diagram of the experiment. B: Samples of activities of radial, ulnar, and median nerves responding to acupuncture-like stimulation of a forepaw. C: Sample recordings of CBF in the parietal cortex before and after severing the somatic afferent nerves in spinalized rats (modified from Uchida et al., 2000, 2002).
2.2.2. Group I+II afferent fibers

EA stimulation applied to the hindpaw induced pupillary dilation (Ohsawa et al., 1997) (Fig. 3C). The response was obtained with stimulus intensities above 0.5 mA and the magnitude of the response further increased with stronger stimulation (Fig. 3B). This study showed that group II afferent nerves in the hindpaw are involved in pupil dilation induced by EA stimulation (Fig. 3A, B).

2.2.3. Group I+II+III afferent fibers

The magnitude of the response of above-mentioned pupillary dilation further increased with stronger stimulation above the threshold of intensity for group III fibers (Ohsawa et al., 1997). EA stimulation of the hindpaw at a stimulus strength sufficient to excite the group III afferent fibers produced an increase in skeletal muscle blood flow (MBF) in biceps femoris of the hindlimbs, accompanied by an increase in systemic arterial blood pressure in anesthetized rats (Noguchi et al., 1999a; 1999b), an increase or decrease in the secretion rate of catecholamines (Mori et al., 2000), and an increase in cortical cerebral blood flow (Uchida et al., 2000), whereas excitation of group I and group II fibers was ineffective on these parameters.

EA stimulation of the hind leg at a stimulus strength sufficient to excite the group III afferent fibers produced responses of either increases or decreases in the secretion rate of catecholamines, whereas excitation of group I and group II fibers was ineffective (Mori et al., 2000).

2.2.4. Group I+II+III+IV afferent fibers

For the above described effect of EA stimulation on visceral function (pupillary dilation, increase in MBF, pressor response, decrease in RBF, increase in catecholamine secretion, and increase in CBF), the magnitude of the response was further increased with stronger stimulation above intensity of threshold for group IV fibers (Ohsawa et al., 1997; Noguchi et al., 1999a,b; Mori et al., 2000; Uchida et al., 2000). Therefore, activation of groups IV afferent fibers during acupuncture stimulation appears to be capable for producing various autonomic functions.

2.2.4.1. Skin and muscle. EA stimulation of a hindpaw causes an excitatory response, while that of hind leg causes either excitatory or inhibitory responses of adrenal medullary functions, even if both group III and IV somatic afferent fibers are stimulated (Mori et al., 2000). Mori et al. (2000) speculated that afferents innervating the skin and muscles may have different reflex influences on the functions of some visceral organs observed for the adrenal medulla. Group III and IV afferents from the skin seem to have more excitatory reflex effects, while group III and IV afferents from the muscle may have a diverting
effect that may depend on the animal’s condition, probably the depth of anesthesia at least in these anesthetized animal experiments.

3. Regulation of motor function

It has been reported that acupuncture stimulation diminished the skeletal muscle tone induced by various motor reflexes. Especially in the case of the muscle under continuous tonic contraction, it is considered that the inhibition of the muscle tone by acupuncture stimulation may be related to pain reduction. It has been clarified that somatic afferents are involved in effects on motor reflexes.

3.1. Manual acupuncture

3.1.1. Forearm

Homma et al. (1980) examined the effects of manual acupuncture on the tonic finger flexion reflex caused by the mechanical vibration of the index finger. Acupuncture stimulation of forearm (Waikuan, TE5) inhibited the vibration-induced finger flexion reflex (Fig. 4, Table 2).

3.1.2. Hindleg

Needling point Zusanli (ST36) on the right hindlimb had a significant suppressive effect on the jaw movement response (JMR) and the electromyogram of left digastrics muscle (dEMG) induced by left peroneal nerve stimulation (Lu, 1983). This effect is weakened or abolished by sectioning the right peroneal nerve.

Manual acupuncture applied to the hindpaw clearly inhibits the jaw-opening reflex (JOR) elicited by the electrical stimulation of the tongue, and this effect was completely abolished after the topical application of capsaicin to the sciatic nerve trunk (Okada et al., 1996). This result suggests that the capsaicin-sensitive thin afferent fibers may play an important role in the inhibition of the JOR induced by acupuncture. The inhibition of the JOR was elicited by manual acupuncture stimulation of various segmental areas such as the nose, auricle, forepaw, abdomen, hindleg and hindpaw.

3.2. Electro-acupuncture

The effects of EA stimulation on several motor functions were studied using anesthetized rats (Table 2). EA stimulation applied to

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<tr>
<th>Stimulation site</th>
<th>Afferent</th>
<th>Response</th>
<th>Reference</th>
</tr>
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<tbody>
<tr>
<td>Manual acupuncture</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forepaw (Waikuan)</td>
<td>Not determined</td>
<td>Vibration-induced finger flexion reflex ↓</td>
<td>Homma et al. (1980)</td>
</tr>
<tr>
<td>Hindlimb</td>
<td>Capsaicin-sensitive afferent fibers</td>
<td>Jaw-opening reflex induced by tongue stim. ↓</td>
<td>Okada et al. (1996)</td>
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</tr>
<tr>
<td>Electro-acupuncture</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forepaw (Hoku)</td>
<td>Aδ</td>
<td>Jaw-opening reflex induced by tooth pulp stim. ↓</td>
<td>Toda (1978)</td>
</tr>
<tr>
<td>Hindleg</td>
<td>Aδ</td>
<td>Tail flick reflex ↓</td>
<td>Tsuruoka and Yamakami (1986)</td>
</tr>
<tr>
<td>Forepaw (Hoku)</td>
<td>Aδ, C</td>
<td>Tail flick reflex ↓, hindlimb withdrawal induced by heat stim. ↓</td>
<td>Kawamura et al. (1992)</td>
</tr>
<tr>
<td>Forepaw</td>
<td>Capsaicin-sensitive afferent fibers</td>
<td>C-fiber reflex of the biceps femoris muscle evoked by electrical stim. of hindpaw ↓</td>
<td>Zhu et al. (2004)</td>
</tr>
</tbody>
</table>

↓: decrease.
hindlimb or forepaw induced stimulus intensity-dependent inhibition of jaw-opening reflex (Toda, 1978; Kawakita and Funakoshi, 1982), tail flick reflex (Tsuruoka and Yamakami 1986; Kawamura et al., 1992), C-fiber reflex (Zhu et al., 2004).

3.2.1. Group I afferent fibers

There have been no evidence showing that an effect of acupuncture on motor reflexes is induced by group I afferent fibers.

3.2.2. Group I + II afferent fibers

Toda (1978) recorded the responses of digastrics EMG (dEMG) evoked by stimulation of the tooth pulp, and demonstrated that EA stimulation to the forepaw (HoKu, L14) suppressed the dEMG responses (Fig. 5). This suppression was obtained with stimulus intensities sufficient to excite Aβ afferent fibers, but below the threshold for Aδ fibers (3T). After the median and radial nerves were sectioned, the suppression of the dEMG was not observed. From these results, this study showed that Aβ afferent fibers in the forepaw is involved in the dEMG response by EA.

Tsuruoka and Yamakami (1986) reported that Aδ afferent nerve impulses elicited by EA stimulation at the Zusanli (hindlimb) or the Hoku (forepaw) point suppressed the tail flick reflex, which is a withdrawal response to the application of noxious heat to the tail.

3.2.3. Group I + II + III afferent fibers

Kawakita and Funakoshi (1982) demonstrated that EA of the hindleg suppressed the jaw-opening reflex in lightly anesthetized rats. They observed similar suppression of jaw-opening reflex by activation of Aδ fibers in peripheral nerve (common peroneal nerve) with triangular pulses, but by activation of Aβ fibers was almost ineffective (Kawakita and Funakoshi, 1982). From these results, this study showed that Aδ fibers are involved in suppression of jaw-opening reflex by EA.

Zhu et al. (2004) reported that the C-fiber reflex electromyographic (EMG) signals of the biceps femoris muscle elicited by electrical stimulation of the sural nerve receptive field were inhibited by EA stimulation to ipsilateral hindlimb (Zusanli) with intensities for activating myelinated afferent fibers (moderate inhibition with 0.6–0.8 TAo, and strong inhibition with TAo range).

3.2.4. Group I + II + III + IV afferent fibers

The magnitude of the response of above-mentioned C-fiber reflex inhibition increased with stronger EA stimulation above the threshold of intensity for group IV fibers (Zhu et al., 2004).

The EA applied to the forepaw elevated the percent latency for hindlimb withdrawal after the animal was placed on a hot plate. The effect of the EA disappeared after treatment of the same forepaw with the capsaicin (Kawamura et al., 1992). Therefore, it is most probable that substance-P-containing C-fibers, whose nerve conduction was blocked by treatment with capsaicin, convey the information for EA.

4. Single afferent nerve fibers activated by manual acupuncture stimulation

There have been a few reports demonstrating the activation of different populations of afferent nerve fibers during manual acupuncture stimulation using recording technique of unitary discharge activities of nerve fibers. For example, Wang et al. (1985) reported that groups II, III and IV fibers were activated during manual acupuncture in humans, while Zhou et al. (2005) reported that groups II and IV fibers were activated in rats. However, in these reports the unitary discharge activity of nerve fibers during acupuncture was recorded from the peripheral nerve, thus making it difficult to conclude that activated group IV fibers recorded were purely somatic afferent fibers or were antidromically activated sympathetic postganglionic efferent fibers.

Recently we examined, using single unit nerve recording techniques in anesthetized rats, which specific population of afferent nerve fibers (groups I, II, III and IV) in the dorsal roots at the 4th or 5th lumbar segments (L4 or L5) were activated during manual acupuncture stimulation.

![Fig. 6. Manual acupuncture needle stimulation to the hindlimbs activated single unit afferent in the spinal dorsal roots belonging to groups I, II, III and IV fibers. Sample recordings (A) and summarized results (B) of the activity of single unitary afferents in the spinal dorsal roots. B: Dots represent individual values. Each column and vertical bar represents the mean ± SEM. *p < 0.05, **p < 0.01 (modified from Kagitan et al., 2005).](image-url)
Recording from the dorsal spinal root eliminates the possibility of recording antidromically activated afferent nerves, thus specifically defining the groups of afferent fibers activated. For this purpose we inserted an acupuncture needle into the skin and underlying muscles around the Zusanli acupoint area in the hindlimbs of anesthetized rats, and twisted it manually to record activity from single nerve fibers from a dissected nerve branch of the 4th or 5th lumbar spinal dorsal roots, which contain purely afferent nerve fibers a portion of which originate from the hindlimb (Fig. 6). A single afferent fiber activated by acupuncture stimulation was identified by the identical shape of the discharge spikes during stimulation and during electrically evoked action potentials induced by single pulse electrical stimulation of the sciatic nerve. The conduction velocity of each nerve fiber recorded was used to determine the classification of afferents as belonging to groups I, II, III or IV (Fig. 6A).

A total of 35 units were intentionally recorded from all animals in order to include all 4 afferent fiber groups. Units were spontaneously silent in the absence of stimulation, while all units responded to ipsilateral manual rotation of the acupuncture needle. The conduction velocity of all 35 units ranged from 0.8 to 86.0 m/s, thus belonging to groups I–IV fibers. The mean conduction velocity of groups I, II, III and IV were 57.9 m/s (n = 13), 42.9 m/s (n = 11), 10.3 m/s (n = 6) and 1.2 m/s (n = 5), respectively. The mean discharge rates during acupuncture stimulation of groups I, II, III and IV afferents were 7.4 Hz, 6.2 Hz, 4.7 Hz and 0.4 Hz, respectively (Fig. 6B). The discharge rates of group IV afferent fibers were significantly lower than those of groups I, II and III afferents. It was concluded that manual acupuncture stimulation to the hindlimbs activated afferent nerve fibers belonging to all four groups of afferents in rats.

It is suggested that all 4 groups of somatic afferents activated by manual acupuncture stimulation will elicit various effects when action potentials are delivered to the central nervous system. It seems noteworthy that the different frequency of discharge recorded among groups I–IV afferents during manual acupuncture stimulation is important in explaining the practical selection of high and low frequencies during EA.

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References


