Short- and long-term modulation of upper limb motor-evoked potentials induced by acupuncture

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Abstract

The aim of this study was to investigate in humans the effects of acupuncture upon upper-limb motor-evoked potentials (MEPs), elicited by transcranial magnetic stimulation of the primary motor cortex. It is known that peripheral sensory stimulation can be used to induce short- and long-term changes in motor cortex excitability. Data show that the simple insertion of the needle is an adequate somatosensory stimulus to induce a significant modulation of MEP amplitude, the sign of which (facilitation or inhibition) is specific to the investigated muscle and to the point of needle insertion. Moreover, MEP changes in upper-limb muscles are also observed following needling of lower-limb sites, revealing the presence of long-distance effects of acupuncture. Finally, the modulation in muscle excitability considerably outlasts the time period of needle application, demonstrating the induction of long-term plastic changes in the central nervous system. In addition, results have shown that the effects on muscle excitability are not restricted to the stimulation of well-coded acupoints, as described in traditional Chinese medicine, but they can also be induced by needling of nonacupoints, normally not used for therapeutic purposes. The possible neuronal mechanisms underlying the observed effects of acupuncture are discussed in relation to the available neurophysiological data regarding the interlimb reflexes and the changes in the representational cortical maps induced in humans by a prolonged somatosensory stimulation.

Introduction

Acupuncture is a 1000-year-old therapeutic technique of traditional oriental medicine. In western countries it has gained increasing popularity in health care over the past few decades. Although mechanisms of its action remain elusive, the National Institute of Health Consensus Conference (NIH Consensus Conference, 1998) concluded that acupuncture is an efficacious alternative therapy in postoperative and chemotherapy-induced nausea and vomiting, as well as in postoperative dental pain, and that it may be helpful in treating many other medical conditions.

According to traditional Chinese medicine, functional organic systems are connected through a network of channels, called ‘meridians’. The insertion of acupuncture needles in specific acupoints along the meridians would have a therapeutic benefit on nearby or distant organs, by regulating energetic imbalances within the organism. However, recent neuropharmacological and neuroimaging data have shown that many of the effects of acupuncture might be mediated by the activation of disease-related areas within the central nervous system. For example, stimulation of analgesic acupoints induces the release of different kinds of opioid neuropeptides (Han & Terenius, 1982; Han, 2003) and the activation of many areas of the limbic/paralimbic systems involved in pain mediation (Hui et al., 2000; Biella et al., 2001; Hsieh et al., 2001). Furthermore, stimulation of eye-related (Cho et al., 1998; Siedentopf et al., 2002; Li et al., 2003a) and language-related acupoints (Cho et al., 2000; Li et al., 2003b) has been shown to activate cortical areas implicated in vision and auditory/language processing, respectively.

An interesting tool for investigating acupuncture effects on activity of the central nervous system is the study of motor cortex excitability. This approach arises from the consideration that if multiple brain areas are activated by acupuncture, this must be the consequence of the stimulation of somatosensory afferent fibres, produced by needle insertion. It is well known that peripheral sensory stimulation induces short- and long-term changes in motor cortex excitability. In fact, the stimulation of skin or muscle nociceptive fibres in the distal upper limb has an inhibitory effect on motor-evoked potentials (MEPs), induced by transcranial magnetic stimulation (TMS) of the primary motor cortex (Koalker et al., 1998, 2001; Valeriani et al., 1999; Farina et al., 2001; La Pera et al., 2001; Svensson et al., 2003). This inhibition is specific to the muscles adjacent to the painful area, given that it is not present or becomes excitation in more proximal muscles. Conversely, a prolonged nonpainful stimulation of peripheral nerves induces a long-term increase in excitability in the motor cortex representation of the corresponding muscles (Mariorenzi et al., 1991; Hamdy et al., 1998; Ridding et al., 2000, 2001; Kaelin-Lang et al., 2002; Charlton et al., 2003). These effects are also very specific and are accompanied by topographic changes in the related representational cortical maps.

The aim of this study was to ascertain whether insertion of an acupuncture needle constitutes an adequate stimulus of somatosensory afferents, in order to induce changes in the excitability of cortical and/or spinal motor areas. This issue has been investigated by studying the acupuncture-induced modulation of MEPs in various muscles of the upper limb, after TMS of the contralateral primary
motor cortex. How the sensory fibre stimulation or the changes in motor excitability, induced as a result of needle insertion, relate to the therapeutic effects of acupuncture is far beyond the scope of the present paper and cannot be addressed by the experimental approach utilized here. Instead, we were particularly interested to ascertain whether acupuncture is able to induce long-lasting plastic changes in cortical/spinal excitability, as with those reported to occur after the prolonged stimulation of somatosensory afferent fibres, by verifying the persistence of changes in MEP amplitude after needle extraction. In addition, the specificity of acupoint effects has also been addressed by comparing the responses induced by needle insertion in well-coded analgesic points of traditional acupuncture with those induced by stimulation of nonacupoints, normally not used for therapeutic purposes. Finally, because in oriental medicine acupoints are believed to exert effects on body parts located at a considerable distance, we investigated whether MEP amplitude of hand and wrist muscles is also affected by acupuncture applied to distant cutaneous areas of the lower extremities.

Materials and methods

Subjects

Fifteen healthy adult volunteers (eight female and seven male, ages 19–46 years, mean age 28.9 years), with no history of head trauma or neurological disease, participated in the study, and all gave written informed consent. All procedures were conducted in accordance with the ethical guidelines set forth by the Helsinki declaration. All subjects were Europeans and right-handed, as measured by the Edinburgh handedness inventory. They were all naïve to acupuncture stimulation, except three participants who had previous experience and cultural exposure to acupuncture.

Stimulation and recording

Subjects lay comfortably in a supine position, with their head immobilized by a polystyrene-bead vacuum splint, moulded on the neck and rear part of the head. Acupuncture needling was performed by experienced acupuncturists under aseptic conditions. Disposable sterilized Hawato needles (Suzhou Medical Appliance Factory, China) were used, measuring 0.30 × 25 mm for hand acupuncture and 0.26 × 40 mm for lower limb acupuncture. Two distinct sites for acupunctures were chosen on both upper and lower limb: a well-known classical acupoint, as described in traditional Chinese medicine, and a nonacupoint. On the upper limb, acupoint LI4 (Hegu) at the region of the first dorsal interosseus space of the left hand was used (Fig. 1A). This is one of the most frequently exploited points in Chinese acupuncture, of prominent analgesic efficacy. As a hand nonacupoint (hereafter HNA), we chose a site in the proximal third of the thenar eminence on the left side, at a distance of 2 cm from the radio-carpal joint. Experiments with upper-limb acupuncture were conducted on ten subjects. For lower-limb acupuncture, we used acupoint ST38 (Tiaokou) situated laterally to the anterior crest of the tibia, about midway along the course of the tibialis anterior muscle (Fig. 1B). This is another classical analgesic acupoint, which is often utilized to treat shoulder pain. As a lower-limb nonacupoint, we chose a site on the lateral aspect of the thigh (TNA), placed between the vastus lateralis and the biceps femoris, midway between the transverse popliteal crease and the highest point of the great trochanter. Eight subjects participated in the experiments with lower-limb acupuncture, which was performed either to the left or to the right side in equal numbers (two subjects were tested on both sides). Three subjects were involved in both upper- and lower-limb experiments. In both upper- and lower-limb groups, all subjects underwent needling of both acupoints and nonacupoints in different experimental sessions, in a randomized order. The depth of needle insertion in the tissue was ~1 cm at LI4 and HNA, and ~2 cm at ST38 and TNA.

Surface electromyograms (EMG) were simultaneously recorded from abductor digiti minimi (ADM), first dorsal interosseous (FDI) and flexor carpi radialis (FCR) muscles, ipsilaterally to the acupuncture sites, by means of silver/silver chloride electrodes in bipolar configuration (interdetection spacing of about 2 cm). FDI muscle was not recorded when acupuncture was applied to the LI4 acupoint, because of its proximity to the needling site. Signals were amplified 1000× in the bandwidth 0.2 Hz to 1 kHz. EMG was digitally converted (PCI-MIO-16E-4, National Instruments, Austin, TX, USA) and sampled at 4 kHz on a personal computer. MEP waveforms were logged and analysed off-line by means of custom-written Labview software (National Instruments).

TMS was applied to the motor cortex, contralaterally to the EMG recorded muscles, with a Magstim Super Rapid magnetic stimulator (Mag-1450-00, Magstim Co. Ltd, Whitland, UK), using a figure-of-eight double coil (Ø 70 mm). The coil was orientated at 45° oblique to the sagittal plane, so that the induced current flowed perpendicular to the estimated alignment of the central sulcus. The scalp site at which MEPs were elicited in ADM muscle at the lowest stimulus strength was determined. Once the optimal scalp site was found, the coil was securely fixed in place by means of an appropriate mechanical device. The response threshold was defined as the stimulus intensity at which 5/10 consecutive single stimuli at the optimal site evoked an MEP of at least 100 μV amplitude in the relaxed muscle (Rossini et al., 1994). Stimulus intensity during the entire stimulation paradigm was set at 1.2 times the ADM motor threshold. This stimulation intensity at the optimal scalp site for ADM also evoked MEPs in FDI and FCR muscles in all experimental sessions. However, to ensure that acupuncture effects could be measured against a reliable baseline, FDI and FCR data were included in the analysis only if their MEPs had an amplitude greater than 100 μV in 10/12 stimuli delivered during the control phase of the experimental protocol, before acupuncture needle insertion. This acceptance criterion was always fulfilled by FDI recordings; by contrast, FCR data were rejected in 6/40 experimental sessions. All data from one experiment with LI4 acupuncture had to be discarded for technical reasons. Furthermore, attention was paid that all TMS sequences were performed with subjects keeping their muscles completely relaxed, in the absence of any detectable EMG activity.

MEP amplitude was defined as the peak-to-peak amplitude of the mean response obtained by averaging 12 consecutive TMS trials, delivered with an interstimulus interval of 5 s. This sequence of test stimuli had an overall duration of 1 min and was employed as our standard procedure to measure cortical/spinal excitability to TMS in resting conditions and following acupuncture.

Stimulation protocol

The experimental protocol was designed in order to differentiate the effects induced by the simple needle insertion from those induced by a prolonged needle manipulation, similar to that applied for therapeutic purposes in traditional Chinese medicine. Furthermore, we also wanted to ascertain the existence of long-term changes in cortical/spinal excitability, persisting after needle removal. To this end, we divided the experimental session into four phases (Fig. 1C). In the ‘control phase’, MEP amplitude in resting conditions was measured by
three sequences of test stimuli applied at 3-min intervals. Following a resting period of 3 min, the ‘needle insertion phase’ began by simply inserting the acupuncture needle in the selected site, without applying any kind of manipulation. Changes in muscle excitability to TMS were assessed by means of four sequences of test stimuli delivered at 3-min intervals, starting 1 min after needle insertion. A needle manipulation was then undertaken by the acupuncturist for 15 s, by using the lifting and thrusting technique with no needle rotation. This procedure was repeated after a resting time interval of 15 s, for a total duration of 2 min of alternating manipulation and resting periods. The ‘postmanipulation phase’ followed in which, after a further 2 min of rest, TMS stimulation was applied again by delivering three sequences of test stimuli at 3-min intervals. One minute after the last sequence the needle was removed, marking the beginning of the final ‘postacupuncture phase’. Here, the presence of long-term changes in muscle excitability to TMS was ascertained by measuring the changes in MEP amplitude by four sequences of test stimuli applied at 3-min intervals, starting 2 min after needle removal. The entire stimulation protocol therefore had a total duration of 55 min.

Results

Needling sensation

Subjects well tolerated the acupuncture procedure in all 40 experimental sessions. Needling was experienced as a mild (29 trials) to moderate (seven trials), short-lasting pain sensation (pricking), for all four sites of acupuncture. No sensation at needle insertion was reported in the remaining four cases.

In traditional Chinese medicine, De Qi is a unique sensation of numbness, soreness, heaviness or tingling that develops at the site of acupuncture, often spreading towards nearby cutaneous areas. When
acupuncture was performed along classical meridians (both at LI4 on the hand and at ST38 on the leg) De Qi sensation was reported following needle manipulation in 90% of the experimental sessions. Subjects never described needle manipulation at LI4 or ST38 acupoints as painful.

By contrast, De Qi was never reported during needle manipulation at the two nonacupoints HNA and TNA. Pooling together hand and thigh data, needle manipulation yielded no sensation in four sessions and a moderate but bearable painful sensation in seven sessions. In all other cases, subjects reported a tactile or nonpainful pricking sensation, strictly localized at the needle insertion point.

**Effects of hand acupuncture on MEP amplitude**

Needling of both LI4 and HNA significantly influenced MEP amplitude of both hand and forearm muscles. However, the direction of change and its time course markedly differed depending on the acupuncture site.

Figure 2A shows, as an example, the effects of LI4 acupuncture on the average MEP recordings from the ADM muscle in one representative subject. Each column contains all MEP measurements obtained in the corresponding phase of the experimental protocol. Note the steadiness of the waveform amplitudes during the control phase, as well as within the subsequent phases following needle insertion. A clear decrease in MEP amplitude can readily be observed after needle manipulation, which is maintained also after needle removal.

Figure 3 shows the modulation of mean MEP amplitude across subjects in ADM, FCR and FDI muscles during the different phases of our acupuncture protocol, with separate graphs for the two stimulation sites. Each point represents the group average value, after an intra-subject normalization by the mean MEP amplitude of the three control values recorded before needle insertion. For each phase of the protocol, MEP amplitude was compared with the control values by a two-way ANOVA for repeated measurements (phase and timing-within-phase as factors). No significant principal effects for the timing-within-phase of stimulation or interaction between the two factors were found in all comparisons. The phases for which the test yielded a statistically significant difference \( (P < 0.05) \) with respect to the control are indicated in Fig. 3 by filled symbols. For LI4 acupuncture, neither needle insertion nor its manipulation produced changes in MEP amplitude. However, a highly significant decrease in MEP amplitude was observed after needle extraction in ADM \( (P < 0.001) \). No modulation of MEP amplitude was observed in FCR muscle.

By contrast, a completely different response pattern was observed following HNA acupuncture. Simple needle insertion induced an MEP

![Fig. 2.](image-url)

**Fig. 2.** Average EMG recordings from ADM muscle of two representative subjects, showing the effects of acupuncture at the LI4 and ST38 acupoints on the amplitude of MEPs, evoked by TMS of the contralateral motor cortex. Each trace is the average of 12 responses; trace onsets correspond to the time of delivery of the TMS pulse. For each phase of the experimental protocol, all repetitions of MEP measurements are shown, ordered according to their time sequence from top to bottom. (A) MEP recordings from one subject in an experimental session in which acupuncture was performed at the LI4 acupoint (hand). (B) MEP recordings in a different subject following acupuncture at the ST38 acupoint (leg).
amplitude increase in ADM ($P < 0.05$) and a reduction in FDI ($P < 0.001$). However, these changes were not maintained in the last two protocol phases, i.e. after needle manipulation and extraction. Again, no significant modulation of MEP amplitude occurred in FCR muscle.

**Effects of lower-limb acupuncture on MEP amplitude**
Because acupuncture proved to be very effective in modulating MEP amplitude when applied near the recorded muscle, irrespective of whether the site was or was not a classical acupoint, we investigated whether distant points in the lower limb could also similarly affect hand muscle excitability following TMS. Needling was applied to the anterior surface of the leg on ST38, a commonly used distal acupoint to treat shoulder pain, and to TNA, which was located on the thigh along the long head of the biceps femoris muscle, outside any classical meridian.

As an example, Fig. 2B shows the effects of ST38 acupuncture on the average MEP recordings from the ADM muscle in one representative subject. It can be seen that the simple needle insertion induces a slow build-up in MEP amplitude. This increase in muscle excitability is then maintained also in the postmanipulation phase and following needle extraction.

We performed two experimental series that differed with respect to the side on which lower-limb acupuncture (and muscle recording) was executed. Three-way ANOVA (side, phase and timing-within-phase as factors) yielded no significant left–right difference in MEP amplitude of ADM ($P > 0.5$), FCR ($P > 0.5$) and FDI ($P > 0.1$) muscles, for both ST38 and TNA acupuncture. Therefore, left- and right-side data were pooled together for further analysis.

Figure 4 shows the modulation of mean MEP amplitude across subjects, in the three studied muscles during the different phases of our acupuncture protocol, when needling was performed in the two lower-limb sites. As in Fig. 3, filled symbols indicate a statistically significant difference ($P < 0.05$) in MEP amplitude with respect to the control, as revealed by a two-way ANOVA test for repeated measurements. Again, modulations in MEP amplitude were induced by acupuncture at both ST38 and TNA. In general, an increase in MEP amplitude was observed in all three phases (after needle insertion, manipulation and extraction). However, the amplitude increase observed in FCR never reached statistical significance, in both ST38 and TNA experiments. By contrast, there was a very large MEP facilitation after needle manipulation in ADM ($P < 0.005$) and FDI ($P < 0.0005$) muscles, which was maintained even over the entire last phase after needle extraction.

**Discussion**
**Effects of acupuncture on excitability of upper-limb muscles to motor cortex TMS**
We investigated the effects of acupuncture upon upper-limb MEPs, elicited by TMS of the primary motor cortex. Our study yields a number of remarkable findings. First, the data demonstrate that simple insertion of the acupuncture needle, which produces only a very mild, localized and short-lasting somatosensory stimulation, is sufficient to induce a significant modulation of excitability of the motor pathways that depart from the primary motor cortex. Secondly, changes in MEP amplitude of upper-limb muscles also occur following acupuncture of lower-limb sites, the central afferent projections of which are primarily directed towards areas of the spinal cord and motor cortex, which are located far from the areas that exert a motor control of the affected muscles. Lastly, the observed modulation of muscle excitability can considerably outlast the time period of needle application, demonstrating that acupuncture is able to induce long-term plastic changes in the central nervous system.

Acupuncture effects can hardly be ascribed to nonspecific changes in whole-system excitability, e.g. due to the level of arousal, given that they appear to depend very specifically on the recorded muscle and on the needling point. For example, acupuncture of the lower limb induces a generalized increase in MEP amplitude, which progressively builds up after needle insertion. This MEP facilitation is then steadily maintained after needle manipulation and needle removal. Conversely, changes in MEP amplitude following acupuncture of the hand strongly depend on the stimulation point and on the investigated muscle. Thus, simple needle insertion at HNA induces an MEP facilitation in ADM muscle, but an MEP inhibition in FDI, with no change in FCR. These effects are not maintained after manipulation or extraction of the needle. By contrast, a marked decrease in ADM muscle excitability builds up after needle manipulation at the LI4 acupoint, which is steadily maintained after needle extraction. It should be pointed out that these markedly different MEP modulations occur in spite of the fact that both the LI4 and the HNA cutaneous sites lie on the C6 dermatome and both ADM and FDI motor innervations come primarily from C8–T1 spinal segments.

This observed decrease in ADM muscle response is in agreement with the conclusions of Lo & Cui (2003), the only study in the literature on the short-term modulation of muscular MEPs induced by acupuncture. These authors also found an MEP decrease in ADM, occurring 2 min following needle manipulation at the LI4 acupoint. However, they did not investigate the long-term effects following needle removal and restricted the analysis to only one muscle.

**Acupoint vs. nonacupoint responses**
We also attempted here to address the issue of the specificity of acupuncture effects, by comparing the responses induced by stimulating well-coded analgesic acupoints, as described in traditional
Chinese medicine, with the responses elicited by acupuncture at points located outside classical meridians, i.e. points that are normally not used for therapeutic purposes. Our data clearly demonstrate that both classical acupoints and nonacupoints are similarly effective in modulating MEP responses to motor cortex TMS. Nevertheless, it should be noted that the elicited responses strongly depend on the needling point, as far as it concerns the affected muscles, direction of excitability changes and time course of the effects.

Finding a reliable ‘sham point’ to use in comparison with classical acupoints is a well-known difficulty in all studies on the efficacy of acupuncture treatments. An ideal ‘sham point’ would be an area of skin located at some distance from any known acupoint. However, over 400 points have been described on meridians in traditional Chinese medicine, so that it is hard to identify a site that is not in the immediate proximity of an acupoint or influences it. Accordingly, it is known that points other than those indicated on acupuncture charts can have therapeutic effects and that needling at ‘sham points’ is effective in inducing analgesia in about 33–50% of patients with chronic pain (Richardson & Vincent, 1986).

In this respect, it is interesting to note that functional neuroimaging studies have demonstrated a remarkable overlapping between the brain areas activated by needling at acupoints and nonacupoints (Wu et al., 2002; Yoo et al., 2004), including a number of areas of the pain neuromatrix such as the insula and the anterior cingulate cortex. Furthermore, auditory and visual cortices are activated not only following acupuncture of eye-related and ear-related acupoints, but also after needling of acupoints not implicated in the treatment of eye or language diseases, as well as following acupuncture of nonmeridian points, normally not used in classical acupuncture (Wu et al., 2002; Yoo et al., 2004).

It should also pointed out that in our study modulation of MEP amplitude was not found to be related to the occurrence of a De Qi sensation, as De Qi was commonly reported by the subjects after acupuncture at the LI4 and ST38 acupoints, but was never experienced after needling at nonacupoints.

**Acupuncture-mediated interlimb effects**

Our results have shown that acupuncture in the lower limb induces a marked facilitation of MEP amplitude in upper-limb distal muscles. MEP amplitude of the more proximal FCR muscle is also somewhat increased with respect to control, especially following ST38 needling, but the difference does not reach statistical significance, probably because of the large sample variability. This is an intriguing finding as it shows that a mild and tonic stimulation of somatosensory afferents to the lumbar spinal cord induces a slow build up of excitability in muscles which are innervated by the cervical segments. Moreover, these changes in muscular excitability are plastic, as they are steadily maintained for more than 15 min after needle removal. Whether this increase in MEP amplitude is due to an augmented excitability of the motoneuronal pool in the spinal cord, or reflects changes occurring at the level of the motor cortex, is an issue that cannot be addressed on the basis of our results. However, data from the literature can suggest a possible neuronal substrate to our finding.

There is a growing body of recent experimental evidence that in humans, similarly to quadrupedal animals, cervical and lumbar spinal cord segments are extensively interconnected. Several studies have investigated reflexes from lower-limb sensory afferents onto motoneurons of upper-limb muscles (and vice versa). In particular, large excitatory and/or inhibitory reflexes in upper-limb flexor and extensor muscles of intact subjects have been described after ankle displacement or cutaneous stimulation of the foot (Kearney & Chan, 1979, 1981), and after electrical stimulation of cutaneous afferents from the distal lower limb (Dietz et al., 2001; Zehr et al., 2001). Similarly, lower-limb reflexes are also evoked following stimulation of upper-limb afferents (Sarica & Ertekin, 1985; Zehr et al., 2001; Kagamihara et al., 2003).

Uncertainty exists about the pathways mediating these reflexes. On the basis of the shortest response latencies, Zehr et al. (2001) suggested that cutaneous reflexes interconnect the four limbs through a propriospinal pathway. However, only a minority of the interlimb response latencies fall below 70 ms (Dietz et al., 2001; Zehr et al., 2001), which has been proposed as the shortest possible latency for a transcortical loop (Nielsen et al., 1997). Obviously, the assumption that interlimb reflexes and the increase in upper-limb muscle excitability, induced by lower-limb acupuncture, are mediated by the same neuronal pathways should be taken very cautiously. Furthermore, it should be noted that interlimb reflexes have been primarily described in proximal muscles including FCR (Dietz et al., 2001; Zehr et al., 2001; Kagamihara et al., 2003). By contrast, in our study FCR excitability is only mildly affected by lower-limb acupuncture, the largest effects being recorded in the distalmost muscles, FDI and ADM.

Nevertheless, the existence of spinal and supraspinal interconnections between lumbar and cervical segments, as revealed by the studies on interlimb reflexes, provides a suitable anatomical and neurophysiological substrate to account for the described long-distance effects of acupuncture.

**Long-term effects induced by acupuncture**

A remarkable finding of this study is the demonstration of an acupuncture-induced neurophysiological effect that outlasts the period of needle insertion. In particular, acupuncture at LI4 induces a statistically highly significant MEP reduction in ADM muscle, which is still present 1.5 min after needle removal and does not show any sign of adaptation in four consecutive assessments of MEP amplitude. This MEP inhibition, observed in the mean response of nine different subjects, must therefore be considered to be the result of a long-term reorganization of motor cortex and/or spinal circuitry. Interestingly, a long-term modulation of MEP amplitude in hand muscles was observed also after acupuncture of the lower limb. In fact, a significant MEP facilitation in ADM and FDI muscles persists after needle extraction following stimulation of both ST38 and TNA. This result clearly demonstrates that the mild and tonic somatosensory stimulation produced by acupuncture has the property of inducing long-term plastic changes in the excitability of very distant nervous structures, which exert a motor control upon remote muscles.

Prolonged stimulation of peripheral somatosensory afferents is known to induce in humans a long-term reorganization of the motor cortex (Hamdy et al., 1998; Farina et al., 2001; Ridding et al., 2001; Kaelin-Lang et al., 2002; Charlton et al., 2003; Svensson et al., 2003). In particular, a painful stimulation of upper extremities induces a long-lasting depression of MEPs elicited by motor cortex TMS in upper-limb distal muscles (Svensson et al., 2003) and a short-lasting facilitation in the ipsilateral biceps brachii (Kofler et al., 1998, 2001). Conversely, a facilitation of MEPs has been described following a nonpainful stimulation of peripheral afferents in both pharyngeal muscles (Hamdy et al., 1998) and hand muscles (Ridding et al., 2000, 2001; Kaelin-Lang et al., 2002; Charlton et al., 2003). Furthermore, extended plastic changes in the cortical maps, which persist for hours (Stefan et al., 2000) or days (McKay et al., 2002) after the end of the
stimulation sessions, have been described to occur following a prolonged combined stimulation of the peripheral nerve and the motor cortex with TMS.

Our results on the long-lasting effects of acupuncture can be cautiously interpreted in this conceptual framework. The site of occurrence of the neuronal reorganization cannot be ascertained on the basis of our data, as the amplitude of MEPs depends on the excitability of both the motor cortex and the spinal cord at the time the TMS pulse is applied. The exact type of afferent fibres that are activated by our procedure is also unknown. Measurements of H-reflex, in order to test changes in spinal cord excitability, are difficult to obtain reliably in upper-limb muscles, except in FCR. Unfortunately, modulations of MEP amplitude in FCR muscle are not statistically significant with our acupuncture protocol, so that this technique to probe spinal cord excitability cannot be usefully applied to our study. Future experiments with F-wave recordings or with measurements of intracortical inhibition with paired-pulse TMS (Kujirai et al., 1993) will be undertaken in order to investigate the level of plastic changes induced by acupuncture.

It should also be mentioned that recent work has demonstrated that subjects must pay attention to the site to which a sustained somatosensory stimulus is applied, in order to induce a sensorimotor reorganization of the motor cortex (Rosenkranz & Rothwell, 2004, 2005). In fact, only in this case was a specific pattern of reorganization produced, in which nearby and distant muscles showed an increase or a decrease of MEP amplitude, respectively. In our study, subjects, although lying relaxed in a supine position, cannot avoid paying attention to the acupuncture site, at least during insertion and manipulation of the needle. In our case, however, long-lasting changes in MEP amplitudes appear to be far more diversified depending on the acupuncture site. For example, a marked MEP increase in hand muscles is induced after needling of very distant sites in the lower limb.

Regardless of the location of the neural reorganization, we are faced with persisting changes in motor excitability induced by a somatosensory stimulation, consisting either in the simple insertion of the needle, as in the case of lower-limb acupuncture, or in a repeated needle manipulation. Unlike findings from previous neurophysiological studies, the plastic changes are here produced by a very localized stimulation of somatosensory afferents and, moreover, can involve muscles that are located far from the site of stimulation. Furthermore, both facilitatory and inhibitory effects can be elicited in the different muscles, depending on the acupuncture site. Although the functional significance of these responses is still far from clear, this study provides further evidence in favour of the capacity of acupuncture to affect nervous functions in a profound and diversified manner.

Abbreviations

ADM, abductor digiti minimi; EMG, electromyogram; FCR, flexor carpi radialis; FDI, first dorsal interosseous; HNA, hand nonacupoint; MEP, motor-evoked potential; TMS, transcranial magnetic stimulation; TNA, thigh nonacupoint.

References


