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# Rapid modulation of cortical proprioceptive activity induced by transient cutaneous deafferentation: neurophysiological evidence of short-term plasticity across different somatosensory modalities in humans

Michele Tinazzi,[1] Tiziana Rosso,[1] Giampietro Zanette,[1] Antonio Fiaschi[1] and Salvatore M. Aglioti[2,3]
[1]Dipartimento di Scienze Neurologiche e della Visione, Sezione di Neurologia Riabilitativa, Università di Verona, Italy
[2]Department of Psychology, University of Rome 'La Sapienza', Via dei Marsi 78, 00185, Roma, Italy
[3]IRCCS, Fondazione Santa Lucia, Roma, Italy

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## Abstract

Single cell recording in non-human primates shows plastic changes of cortical somatic representations across different types of somatic inputs originating from the same peripheral territory. In humans, muscle afferents from first dorsal interosseus are supplied by the ulnar nerve while the cutaneous territory overlying this muscle is supplied by the radial nerve. This peculiar anatomical nervous distribution allowed us to devise an experimental model which provided a unique opportunity to assess, in humans with a non-invasive technique, the functional relationships between cutaneous and muscle afferent inputs originating from the same peripheral territory. We recorded spinal, brainstem and cortical somatosensory potentials evoked by stimulation of muscle afferents of the right first dorsal interosseus before, during and after anaesthetic block of the sensitive branch of the ipsilateral radial nerve. Amplitude of parietal N20 and P27 and frontal N30 somatosensory evoked potential components showed an increase of amplitudes with more profound anaesthesia. Amplitudes returned to pre-anaesthetic values several minutes after anaesthesia. By contrast, spinal N13 and brainstem P14 potentials did not change throughout the experiment. Results show, for the first time in humans, that a transient cutaneous deafferentation may induce rapid modulation of cortical activity evoked by stimulation of muscle afferents originating in the anaesthetic territory.

## Introduction

Somatic perceptions originate from activity in neural pathways that originate from different types of peripheral receptors and target different structures of the central nervous system. The primary somatosensory cortex is organized in cytoarchitectonically and functionally distinct areas (3b, 3a, 1 and 2) which receive afferents from different somatic submodalities (Kaas, 1991; Iwamura, 1998). Studies in non-human primates show that cutaneous afferents convey tactile sensations and are predominantly mapped in areas 3b and 1; in contrast, muscle and joint afferents mediate proprioception and kinaesthesia and are mapped preferentially in area 3a (Powell & Mountcastle, 1959; Heath *et al.*, 1976; Huffman & Krubitzer, 2001). Neurophysiological studies in cats and monkeys show that the described predominance is incomplete because neurons in area 3a also receive cutaneous afferents (Zarzecki *et al.*, 1983; Kang *et al.*, 1985; Cusick & Gould, 1990; Jenkins *et al.*, 1990). Moreover, areas 3b and 1, typically activated by cutaneous inputs, also receive a minority of afferents from muscles and joints (Tanji & Wise, 1981). Human neurophysiological studies also hint at separate representations of proprioceptive and cutaneous inputs in the primary somatosensory cortex. Mima *et al.* (1997), for example, recorded somatosensory evoked potentials (SEPs) from subdural electrodes in an epileptic patient and found that proprioceptive stimuli were preferentially mapped in areas 3a, 1 and 2. By contrast, cutaneous stimulation induced activity mostly in area 3b.

Acute or chronic reduction of somatic inputs may induce functional or structural changes in dedicated subcortical or cortical structures even in the adult brain (Merzenich *et al.*, 1983a,b; Pons *et al.*, 1991; Florence & Kaas, 1995; Faggin *et al.*, 1997; Florence *et al.*, 2000; Jones, 2000). Studies in monkeys with section or anaesthetic block of peripheral sensory nerves show that tactile stimuli delivered to the skin surrounding the deafferented zone induced higher rates of activity in neural structures mapping cutaneous sensations (Merzenich *et al.*, 1983a,b; Pons *et al.*, 1991; Jones, 2000). These results imply that neuroplastic changes are specific for the type of stimulus. Although recent research in non-human primates suggests that plastic changes can also occur across tactile and proprioceptive representations (Jenkins *et al.*, 1990; Recanzone *et al.*, 1992; Xerri *et al.*, 1998, 1999), no studies addressing this issue have so far been carried out in adult humans.

In the present study we used the non-invasive technique of SEPs to assess whether acute deprivation of cutaneous inputs may induce reorganizational changes of non-deprived proprioceptive neural representations. Spinal, brainstem and cortical SEPs following stimulation of muscle afferents of the first dorsal interosseus (FDI) muscle were recorded before, during and after anaesthetic block of the sensitive

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*Correspondence*: Dr Salvatore M. Aglioti, [2]Department of Psychology, as above.
E-mail: salvatoremaria.aglioti@uniroma1.it

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branch of the right radial nerve. It is important to remark here that, while muscle afferents are supplied by the ulnar nerve, the cutaneous territory overlying the same muscle is supplied by the radial nerve.

## Materials and methods

### *Subjects*

Seven right-handed healthy subjects (three men and four women) aged between 24 and 33 years underwent seven SEP recording sets, two before and five after injection of an anaesthetic in the sensitive branch of the right radial nerve. As control conditions, seven sets of SEP were recorded in five right-handed healthy subjects (three women and two men) who did not receive any injections and in five right-handed healthy subjects (three women and two men) in whom 1.5 mL of saline solution were injected at the location corresponding to the right radial nerve at the wrist (see Fig. 1). The penetration of the needle induced a transient, local discomfort in both subjects who received anaesthetic and saline solution. While the no-injection control procedure is adequate to rule out that the pattern observed in the anaesthesia group may be related to spontaneous fluctuations of SEP over different recording sessions, the saline injection procedure is most adequate for controlling for placebo-like effects or non-specific attentional factors related to the injection. Written informed consent was obtained from each subject and the study was approved by the local ethical committee.

### *Somatosensory evoked potential recording procedure*

During SEP recording, subjects lay supine on a comfortable bed in a quiet room. Following standard procedures (Mauguière *et al.*, 1999), subdermal needle recording electrodes (with impedance below 5 kΩ) were placed at the wrist over the right ulnar nerve (bipolar recording), over the spinous process of the sixth cervical vertebra (referred to as the anterior neck) and in the parietal and frontal scalp regions contralateral to the stimulation. Scalp electrodes were referred to the earlobe ipsilateral to the stimulation side. Selective stimulation of muscle afferents was obtained by using a procedure detailed in previous studies (Gandevia *et al.*, 1984; Gandevia & Burke, 1988) and summarized here. Unlike Gandevia and collaborators (Gandevia *et al.*, 1984; Gandevia & Burke, 1988) who recorded only parietal components evoked by stimulation of muscle afferents, the montage of recording electrodes used in the present study allowed us to also record subcortical and frontal components evoked by stimulation of FDI afferents obtained by an insulated tungsten needle microelectrode inserted at the motor point. The motor point corresponds to the position in a muscle at which threshold for evoked contraction is minimal and from which a clear twitch contraction is obtained with stimulation intensities of about 1 mA. The motor point of FDI was preliminarily determined in each subject by inserting a 2-mm diameter stimulating probe electrode in different positions in the muscle. The anode was an uninsulated platinum alloy needle inserted 3–4 cm distal to the cathode, outside the FDI belly. The intensity of stimulation used for SEP recording was 3–6 mA. Stimuli were rectangular pulses of 0.3 ms duration, which were delivered from a constant current source at 1.2 Hz. Stimuli used for SEP recording produced a non-painful twitch contraction of FDI. No radiating cutaneous paraesthesias or sharp sensations localized to joints were induced by the stimuli used for SEP recording. The bandpass was 5–1500 Hz with an analysis time of 50 ms.

### *Induction of anaesthesia*

Muscle afferents of FDI are supplied by the ulnar nerve, while the cutaneous territory overlying the same muscle is supplied by the radial nerve (see Fig. 1). This peculiar anatomical distribution offers a unique opportunity to assess in humans the functional relationships between cutaneous and muscle afferent inputs originating from the same peripheral territory. Transient deafferentation of the skin overlying the right FDI muscle was obtained by injecting local anaesthetic (1–1.5 mL of 2% lidocaine) at the same location of the right radial nerve at the wrist (see Fig. 1). Complete anaesthesia of the skin overlying the FDI was obtained in all subjects within about 10–20 min after injection. Remarkably, muscle afferents from FDI were not

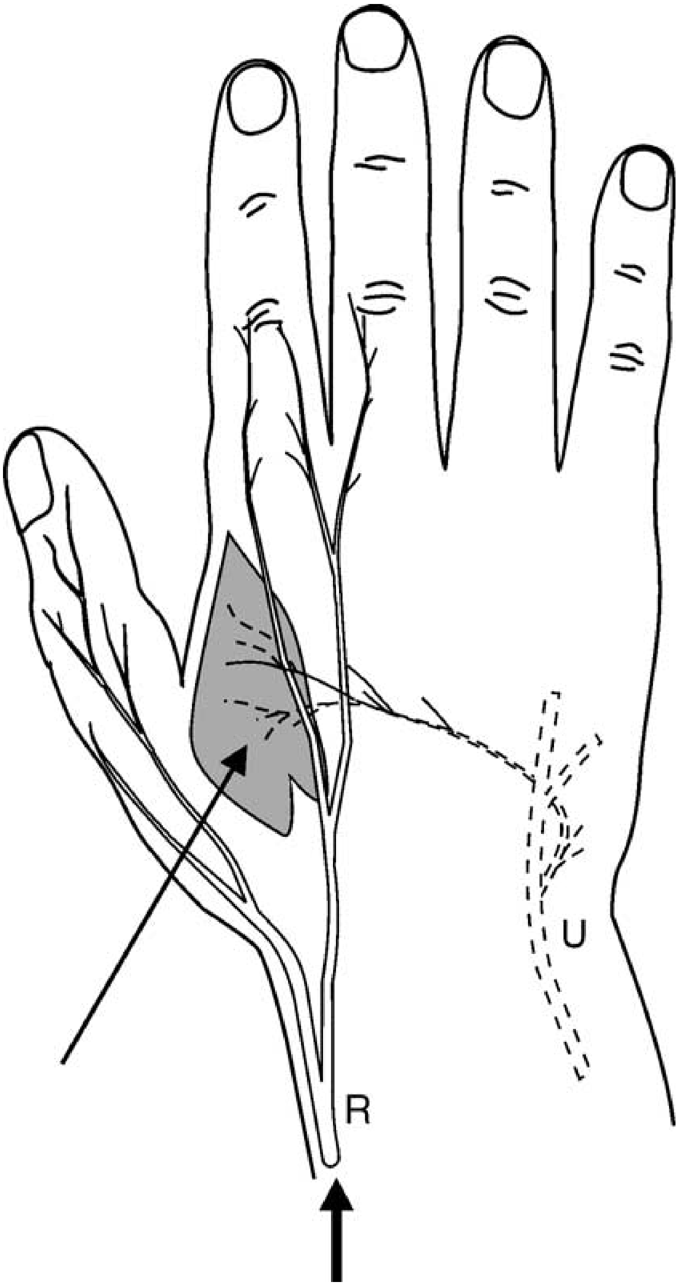

FIG. 1. Schematic showing that the peripheral innervation of first dorsal interosseus (FDI) muscle is supplied by the ulnar nerve and the cutaneous innervation of the skin overlying the same muscle is supplied by the radial nerve. The short, thick arrow indicates the locus of injection of anaesthetic (or saline) in the region of the radial nerve. The long, thin arrow indicates the motor point of FDI (which typically corresponds to the junction of the proximal third with the distal two-thirds of the muscle belly) used for evoking potentials related to muscle stimulation. R, radial nerve; U, ulnar nerve.

affected by the pharmacological block, this muscle being supplied by the ulnar nerve.

Anaesthesia in the territory of the sensory branch of the radial nerve distal to the injection was ascertained by clinical and electrophysiological evidence of abolition of sensory function (see below). Two sets of SEP responses (sets 1 and 2) were recorded over the 30-min period preceding the anaesthetic block, two sets (sets 3 and 4) during the period of complete anaesthesia, two sets (sets 5 and 6) during the recovery phase and one set (set 7) after the effects of anaesthesia had completely faded away. The effects of anaesthesia disappeared completely within about 75–95 min of injection. Each set of SEP responses was obtained from averages of 700 artefact-free trials. Intervals between the different sets used in the control groups were similar to those used in the anaesthesia group.

The pattern of potentials evoked by cutaneous stimulation typically shows the following components: the N13 potential recorded at Cv6 originating in the dorsal horn of the cervical spinal cord (Desmedt & Cheron, 1981); the far-field P14 potential recorded over the parietal and frontal electrodes which presumably originates from the cuneate nucleus (Desmedt & Cheron, 1981); the N20 and P27 potentials recorded over the parietal region contralateral to the stimulation side which are thought to arise from primary somatosensory cortex (Desmedt *et al.*, 1987; Allison *et al.*, 1991) and the N30 potential recorded over the contralateral frontal region. It is important to underline that the origin of this component is still controversial. While it has been suggested that the N30 component may arise from multiple generators located in the frontal lobe (Mauguière *et al.*, 1983; Desmedt *et al.*, 1987), more recent studies seem to indicate that this component is more likely to originate from the posterior wall of the central sulcus (Allison *et al.*, 1991).

Only a minority of previous studies have reported SEPs evoked by electrical stimulation of muscle afferents (Gandevia *et al.*, 1984; Gandevia & Burke, 1988; Restuccia *et al.*, 2002). These studies determined two cortical components analogous to N20 (referred to as N1 by the authors) and P27 (referred to as P1 by the authors). Differences in the montage of electrodes allowed us to detect in each recording set not only N20 and P27 potentials but also three other components evoked by stimulation of muscle FDI afferents, namely one cortical component recorded over the frontal electrode (with latency and morphology similar to the N30 potential evoked by cutaneous stimulation) and two subcortical components (with morphology and significance analogous to the N13 and P14 components evoked by cutaneous stimulation). Relevant to our procedure is the result that potentials evoked by electrical stimulation of the median nerve at the wrist and electrical stimulation of deep proprioceptive input show the same distribution on the scalp (Restuccia *et al.*, 2002). Potentials evoked by proprioceptive stimulation were identified on the basis of latency, polarity and scalp distribution by an individual who was expert with SEP analysis and who, moreover, was naive as to the experimental hypothesis. Amplitudes were measured from the preceding peak (peak-to-peak) and latencies were measured at the peak of each component. Amplitudes were entered in five separate analyses of variance (ANOVA), one for each component. The main factor of each analysis was the SEP recording set which had seven levels (pre-injection sets 1 and 2, post-injection sets 3, 4, 5, 6 and 7). Post-hoc multiple comparisons were made by using the Newman–Kuels test. Similar ANOVAs on latency values did not bring about any change in the injected and non-injected groups. Thus, latency values will not be further considered.

Peripheral orthodromic potentials produced by motor-point stimulation of FDI were recorded in each set by using needle electrodes inserted at the ulnar side 2 cm proximal to the wrist joint. This orthodromic afferent volley showed no changes in latency or amplitude in the different recording sets thus suggesting that the magnitude of the signal delivered to and entering the central nervous system remained stable throughout the recording sets (see, for example, Figs 2D and 3D).

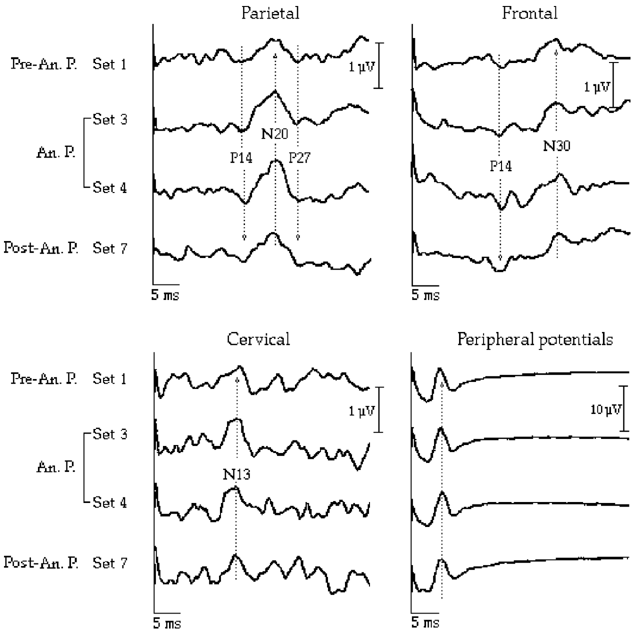

FIG. 2. Profile of potentials evoked by stimulation of the muscle afferents of the right first dorsal interosseus (FDI) in four of the seven recording sets in a representative subject from the anaesthesia group (subject 1). Set 1 was recorded before injection of anaesthetic in the region of the sensitive branch of the right radial nerve, 2 cm proximally to the wrist. Sets 3 and 4 were recorded when anaesthesia was more profound. Set 7 was recorded when the effects of anaesthesia, as inferred from clinical and neurophysiological examination, had completely faded away. (A) Brainstem P14 potential and the N20 and P27 potentials as recorded at the parietal electrode. (B) P14 brainstem potential and the N30 cortical potential as recorded at the frontal electrode. (C) Spinal cord N13 potential as recorded at the cervical electrode. (D) Absence of any modulation of peripheral potentials evoked by afferent stimulation of FDI muscle recorded at the ulnar side of the wrist.

Peripheral antidromic sensory potentials were produced by supramaximal stimulation of the right radial nerve at the wrist about 2 cm proximally to the locus of injection. These antidromic sensory nerve potentials were detected through ring electrodes placed around the right thumb. Deepness of tactile anaesthesia was checked by means of Q-tip strokes delivered on the skin region overlying the right (anaesthetic) or left (normal) FDI. Before injection, tactile sensations induced by these stimuli were identical on both sides. Right-sided stimuli went undetected in the period before recording sets 3 and 4. Right-sided stimuli were detected but reported as less intense than those delivered on the homologous left region before recording sets 5 and 6. Set 7 was recorded when left and right tactile stimuli were perceived as identical. A similar assessment of tactile sensitivity was also carried out in the control groups. Based on the clinical examination of tactile sensitivity, measurements of peripheral potentials were performed before recording set 1 (pre-anaesthesia), immediately before set 3 (complete anaesthesia) and immediately before set 7 (complete recovery phase). Antidromic peripheral potentials had similar amplitude before sets 1 and 7. These potentials were abolished before set 3.

## Results

Spinal N13 potential recorded at the cervical electrode, brainstem P14 potential recorded over the scalp electrodes, parietal N20 and P27 and frontal N30 components were identified. Examples from two

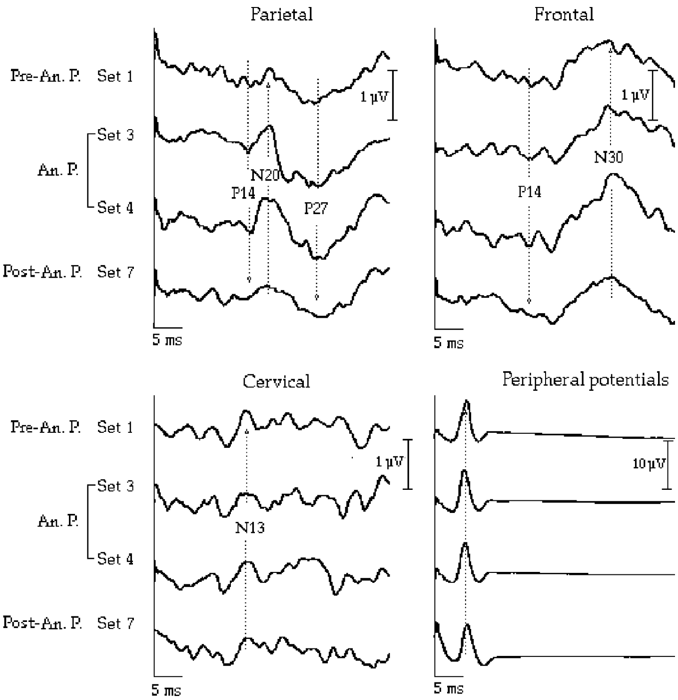

FIG. 3. Profile of peripheral and central potentials evoked by stimulation of muscle afferents of the right first dorsal interosseus in four of the seven recording sets in a representative subject (subject 2) from the anaesthesia group. Legend as for Fig. 2.

representative ‘anaesthetic injection’ subjects of amplitude of SEP responses during the different recording sets are provided in Figs 2 and 3.

Figure 4 shows the average amplitude of the different components in the different SEP recording sets for the seven subjects who underwent injection of anaesthetic.

A series of repeated measures ANOVAs, on the amplitude of each SEP component, was carried out. Each ANOVA had the recording set (with seven levels) as main factor. ANOVA showed a clear significance of the factor Set for all of the three cortical components. The parietal N20 component was significant ($F_{1,6} = 8.9$, $P < 0.01$) because, as shown by post-hoc multiple comparisons, amplitudes in set 3 (when anaesthesia was profound) were higher than in sets 1 and 2 (before injection). Moreover, amplitude in set 4 (when anaesthesia was maximally profound) was significantly higher than in all of the other sets ($P < 0.01$). A trend analysis showed that the curve which best fitted the observed distribution was quadratic ($F_{1,6} = 37.5$, $R^2 = 0.58$, $P < 0.01$). This result indicates that the observed temporal modulation of SEP amplitudes was contingent upon the effects of anaesthesia. A similar figure emerged for the parietal P27 component ($F_{1,6} = 7.9$, $P < 0.01$). The SEP amplitudes in set 3 showed a tendency to be smaller than in set 4 ($P = 0.07$) and higher than in set 5 ($P = 0.09$), when anaesthesia started to fade away. Moreover, amplitudes in set 3 were significantly higher than in all of the other sets ($P \leq 0.01$). In the same vein, amplitudes in set 4 were significantly higher than in all of the other sets ($P < 0.01$). A trend analysis showed that the curve which best fitted the observed distribution was quadratic ($F_{1,6} = 36.7$, $R^2 = 0.67$, $P < 0.001$). Analysis of the frontal N30 component showed

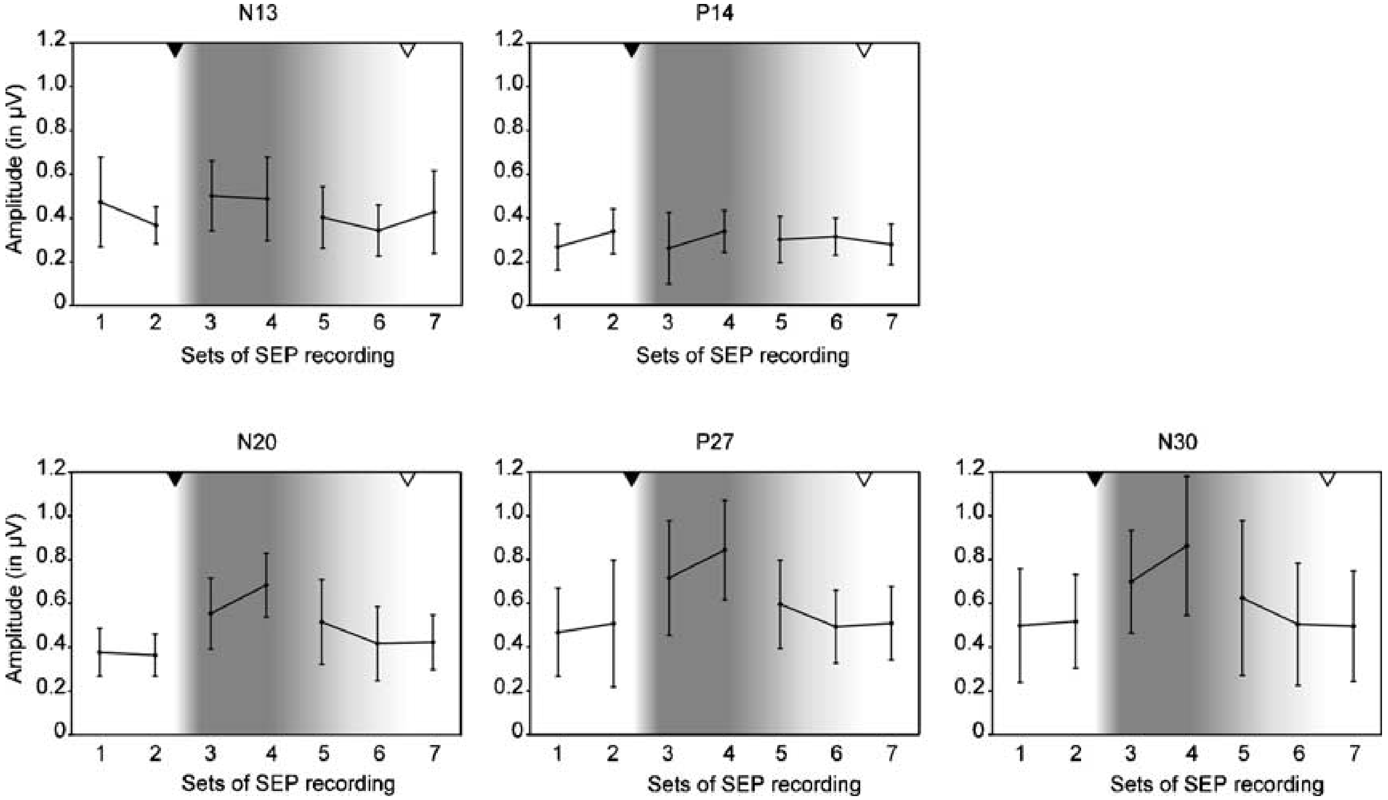

FIG. 4. Mean (and SD) amplitude of subcortical (N13 and P14) and cortical (N20, P27 and N30) somatosensory evoked potential (SEP) components in the different recording sets before (sets 1 and 2) and after (sets 3–7) injection of the anaesthetic in the region of the right radial nerve. Grey areas correspond to periods during which anaesthesia was present. Darker areas indicate deeper anaesthesia. Effects of anaesthesia were assessed immediately before each recording set by means of clinical and neurophysiological testing (see Materials and methods). It should be noted that, in all subjects, set 7 was recorded when the effects of anaesthesia had completely faded.

the significance of the main factor ($F_{1,6} = 11.9$, $P < 0.01$). Post-hoc multiple comparisons showed that SEP amplitudes were similar in sets 3 and 5. Amplitudes in these two sets were significantly smaller than in set 4 ($P < 0.01$) and higher than in all of the other sets ($P \leq 0.01$). Again, amplitudes in set 4 were significantly higher than in all of the other sets ($P < 0.001$). A trend analysis showed that the curve which best fitted the observed distribution was quadratic ($F_{1,6} = 20.7$, $R^2 = 0.62$, $P < 0.01$).

In summary, a clear effect of anaesthesia on the mean amplitudes of cortical components N20, P27 and N30 was observed. The increase of amplitude of cortical SEP components occurred in set 3, recorded after anaesthesia was complete. Maximal increases were reached in the fourth recording set. The amplitude of cortical SEPs remained slightly enhanced during the first part of recovery from anaesthesia (set 5) and then returned to pre-anaesthetic levels in set 6 and even more in set 7. Remarkably, changes of amplitudes contingent upon anaesthesia were observed in all subjects.

It is important to remark that ANOVA on the amplitude of spinal N13 and the brainstem P14 potentials did not disclose any significant effect. Indeed, the factor recording Set was as follows: $F_{1,6} = 1.9$, $P = 0.10$ for N13 and $F_{1,6} < 1$ for P14.

No changes of SEP amplitudes were observed in the five non-injected subjects and in the five subjects injected with saline solution (see Fig. 5).

It is no surprise that injection of saline solution did not induce any changes of somatic sensations in the cutaneous regions overlying FDI muscle and that no variations of tactile sensitivity across the different recording sets were found in the no-injection groups. It is worth noting that the absence of SEP modulation in the saline injection group rules out the possibility that pain induced by injection, although local and short-lasting, was responsible for the increase of SEP amplitude observed in the anaesthesia group.

## Discussion

The main result of the present research is that an acute deprivation of cutaneous input induced by anaesthesia of one peripheral nerve results in an increase of cortical activity evoked by muscle afferents originating from the same body part. This neuroplastic effect across somatic submodalities is not due to non-specific variables being absent in the no-injection and the saline injection control conditions. Moreover, this enhanced cortical reactivity was rapid and reversible and was not associated with spinal and brainstem changes.

### *Cross-modal and cross-submodal plasticity*

Studies indicate that deprivation of sensory stimuli brings about plastic effects not only within the same sensorimotor or visual modality but also across different modalities (Shimojo & Shams, 2001; Bavelier & Neville, 2002). Both functional imaging and transcranial magnetic stimulation studies in congenitally or early blind Braille readers, for example, reported activation of visual structures during tactile reading tasks (Sadato *et al.*, 1996; Cohen *et al.*, 1997, 1999). Plastic cross-talk across touch and pain in normal humans have been reported in magnetocenphalography studies which demonstrate that, while tactile stimuli sequentially activate peak sources in areas 3b and 1, pain stimuli preferentially activate area 1 (Ploner *et al.*, 2000). Similarly, an increased reactivity to tactile inputs in patients with pain (Tinazzi *et al.*, 2000) and phantom pain (Flor *et al.*, 1995, 1997; Birbaumer *et al.*, 1997) has been reported by using SEPs (Birbaumer *et al.*, 1997; Tinazzi *et al.*, 2000) and magnetoencephalography (Flor *et al.*, 1995, 1997).

The present study revolves around neuroplastic interactions across somatic submodalities. Deep and superficial somatic inputs originating from contiguous body parts are typically sent to the central nervous system by the same peripheral nerves. Proprioceptive afferents from the FDI muscle and cutaneous afferents from the skin overlying this muscle, however, are sent to the central nervous system by different peripheral nerves. We took advantage of this peculiar anatomical organization and were able to induce in humans a highly selective, transient inactivation of the cutaneous somatic submodality in the presence of complete sparing of activity of muscle afferents. Results indicate that the subcortical (N13 and P14) and cortical (N20, P27 and N30) SEP components typically evoked by cutaneous stimulation (Tinazzi *et al.*, 1997, 1998, 2000) can also be evoked by selective stimulation of proprioceptive afferents. Even more important is the result that amplitude of the cortical components evoked by stimulation of FDI muscle afferents was higher during anaesthesia of the skin overlying this muscle. Thus, evidence is provided, for the first time in humans, that short-term plastic changes can occur across different somatic submodalities subserving the same part of the body.

Different regions within the primary somatosensory cortex preferentially map deep (area 3a) or superficial (area 3b) afferents. Neurophysiological studies in animals show that response properties of neurons in the primary somatosensory areas may undergo plastic changes as a consequence of physiological modification of sensory input (Jenkins *et al.*, 1990; Recanzone *et al.*, 1992; Xerri *et al.*, 1998). In monkeys, the task of discriminating tactile frequencies delivered to one hand, for example, induced the emergence of novel neural responses to tactile stimulation in area 3a, a structure in which the vast majority of neurons are usually not responsive to cutaneous stimulation (Jenkins *et al.*, 1990; Recanzone *et al.*, 1992; Xerri *et al.*, 1999). Moreover, such modulation paralleled the disappearance of a large part of the normal proprioceptive representation in area 3a (Recanzone *et al.*, 1992). It is relevant that the reappearance of somatosensory functions abolished by a microlesion of the hand representation in area 3b of adult monkeys parallels the emergence of a new representation of the cutaneous fingertips in area 3a, a region which typically maps proprioceptive inputs (Xerri *et al.*, 1998). These remarkable plastic effects may suggest that cutaneous afferents expand from area 3b to area 3a and take over neurons formerly driven by proprioceptive inputs. It is extremely important to note, however, that both areas 3a and 3b share a minority of ‘convergent units’, i.e. neurons that respond preferentially to muscle and cutaneous stimulation originating from the same part of the body (Hyvarinen & Poranen, 1978; Zarzecki *et al.*, 1983; Kang *et al.*, 1985).

In humans, evidence for at least partly separate representations in the primary somatosensory cortex of cutaneous and deep inputs is provided by an fMRI activation study in which punctate stimulation of one hand activated contralateral cortical regions corresponding to areas 3b, 1 and 2. This stimulation, however, failed to activate area 3a (Moore *et al.*, 2000). Moreover, Mima *et al.* (1997) recorded SEPs from subdural electrodes in an epileptic patient and found that muscle and joint inputs preferentially activate area 3a. By contrast, cutaneous stimulation induces activity mostly in area 3b.

### *Possible mechanisms of cross-submodal somatic plasticity*

The increase of cortical activity evoked by muscle afferent stimulation contingent upon deafferentation of cutaneous inputs reported in the present study effect is equally evident for N20 potential, which originates in area 3b, and P27 potential, which originates in area 1. This result would suggest that the cutaneous deafferentation induced by anaesthesia allows proprioceptive inputs to take over cortical areas typically driven by cutaneous inputs. The increase of proprioceptive activity was also absolutely clear for the N30 potential which, although recorded over the frontal electrode, is likely to originate in the

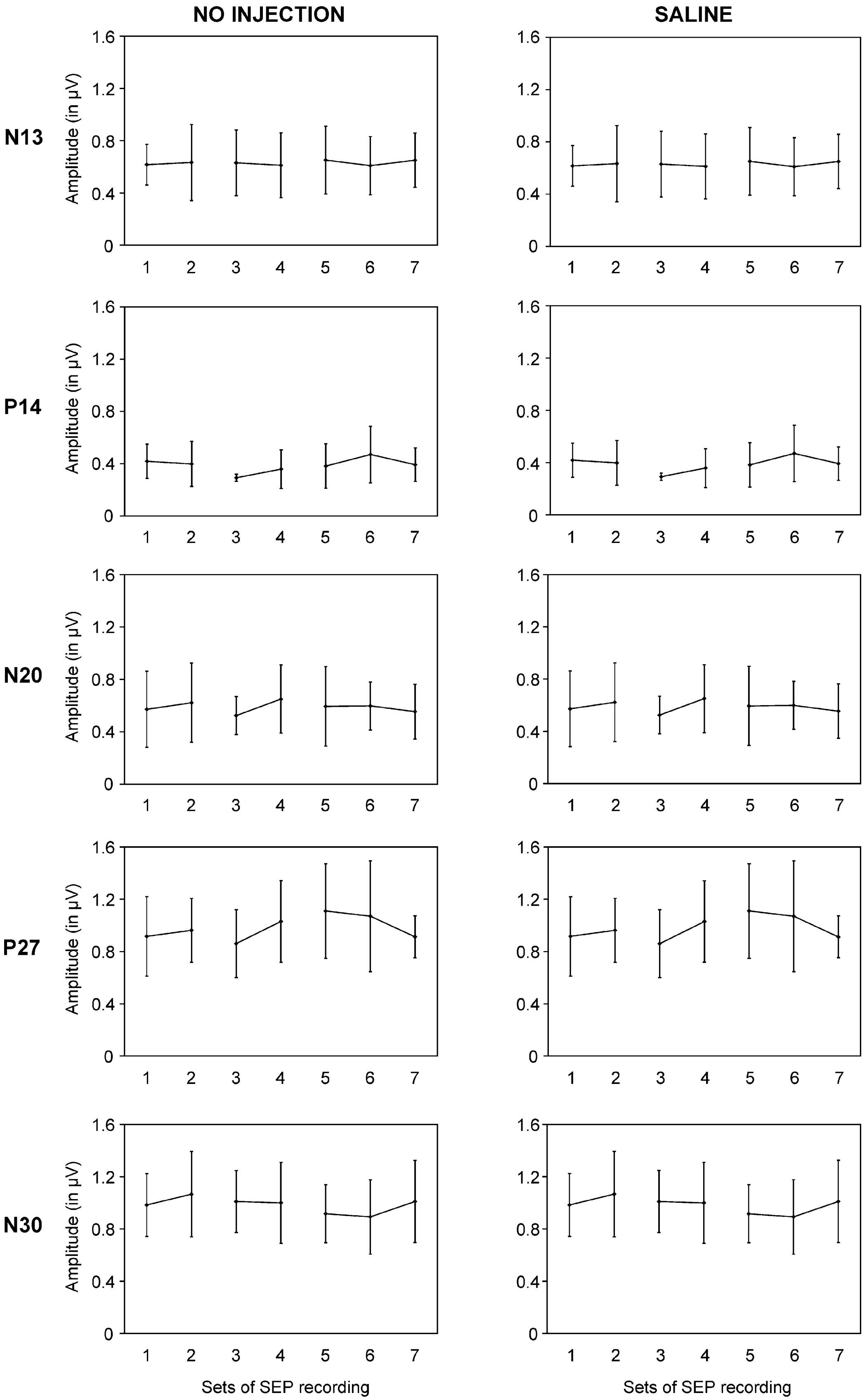

FIG. 5. Mean (and SD) amplitude of subcortical (N13 and P14) and cortical (N20, P27 and N30) components in the no anaesthesia group (left column) and the saline injection group (right column). Numbers from 1 to 7 indicate the seven recording sets. SEP, somatosensory evoked potential.

posterior bank of the central sulcus including area 3a (Allison *et al.*, 1991). Therefore, neuroplastic changes underlying our results are likely to occur within the primary somatic cortex. Neurophysiological studies of the primary somatosensory cortex in animals demonstrate the presence of convergent units, i.e. neurons that specialize for deep inputs but also respond to cutaneous input described in animals. It is possible, for example, that the changes reported in monkeys by Xerri *et al.* (1998) are due to the fact that the training procedure increases the responsivity to cutaneous afferents of neurons in area 3a which were formerly driven by proprioceptive inputs. Neurophysiological evidence for the presence of convergent units also in humans comes from the observation that concurrent stimulation of muscle afferents may have a suppressive effect on cortical potentials evoked by exclusive stimulation of cutaneous afferents originating from the overlying skin (Burke *et al.*, 1981, 1982; Halonen *et al.*, 1988). These convergent neurons may represent a plausible neural basis of the neuroplastic effects reported here. One important implication of this interpretation is that neuroplasticity across somatic submodalities may take place in each areal subdivision of the primary somatic cortex.

It is worth noting that our results expand on monkey studies by showing that similar plastic mechanisms may be called into play following tactile (Xerri *et al.*, 1998) and proprioceptive stimulation (the present study).

The speed and reversibility of the plastic cross-submodal effects described here suggest that these changes may reflect immediate unmasking of pre-existing but physiologically inactive afferents rather than the creation of functional or structural connections between the intact and deprived representations. Electrophysiology studies in squirrel monkeys (Schroeder *et al.*, 1995) demonstrate that neurons in area 3b preferentially map cutaneous afferents from the dorsum of the hand (dominant input) but also cutaneous afferents from glabrous regions of the hand, although much less intensely (latent input). Thus, suppression or reduction of the dominant input may allow the expression of latent inputs. Similarly, the rapid amplification of cortical SEP responses evoked by proprioceptive and joint stimulation reported in the present study may be due to the amplification of response of convergent units which are no longer held in check by cutaneous inputs.

### *Neural loci of cross-submodal somatic plasticity*

Most of the neuroplastic somatic effects consequent to deafferentation appear in the cortex. There is evidence to suggest, however, that changes may also occur at subcortical levels in both animals (Wall & Egger, 1971; Pettit & Schwark, 1993; Florence & Kaas, 1995; Faggin *et al.*, 1997; Florence *et al.*, 2000; Jones, 2000) and humans (Tinazzi *et al.*, 1997, 1998). In the present study deafferentation of the skin overlying the FDI muscle did not induce any significant change of amplitude of cervical (N13) and brainstem (P14) potentials evoked by proprioceptive stimulation of the muscle itself. Hence, another novel result of the present study is that rapid changes of excitability in the primary somatic cortex seem to occur independently of changes downstream in that sensory pathway. It is widely held that the N13 potential reflects post-synaptic neuronal activity of the dorsal horn (Desmedt & Cheron, 1981) and that the P14 potential reflects post-synaptic response of the nucleus cuneatus (Desmedt & Cheron, 1981). Convergence of cutaneous and muscle afferents onto common neuronal populations has also been described in these structures of the somatosensory system (Lynn, 1975; Millar, 1979; Pettit & Schwark, 1993, 1996). Thus, the lack of changes of subcortical components contingent upon anaesthesia cannot be ascribed to the lack of neurons potentially responding to two inputs originating from different submodalities. One may observe that our technique is unable to catch subcortical changes induced by a transient cross-submodal deafferentation. It is important to note, however, that this is not a limitation of the technique *per se* as subcortical neural changes in subjects with chronic deprivation due to carpal tunnel syndrome have been disclosed by using the same technique (Tinazzi *et al.*, 1998). Thus, it is possible that subcortical neural changes occurring after acute deprivation are more subtle than those found following chronic deprivation.

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## Abbreviations

FDI, first dorsal interosseus; SEP, somatosensory evoked potential.

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