Published in final edited form as:

Neurorehabil Neural Repair. 2008 ; 22(5): 477–485. doi:10.1177/1545968308316388.

Influence of Somatosensory Input on Interhemispheric Interactions in Patients With Chronic Stroke

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Abstract

Background—Ischemia-induced cutaneous anesthesia of the healthy hand in patients with chronic stroke elicits transient improvements of motor performance in the contralateral, paretic hand.

Objective—The present study was designed to investigate one of the possible mechanisms underlying this effect.

Methods—The authors evaluated the effects of transient ischemic cutaneous anesthesia of the healthy hand (target intervention) and healthy foot (control intervention) on transcranial magnetic stimulation-induced interhemispheric inhibition from the contralesional onto the ipsilesional primary motor cortex (M1). Ten subjects with chronic, predominantly subcortical stroke with motor impairment were assessed.

Results—Cutaneous anesthesia of the intact hand but not the intact leg resulted in reduction of the inhibitory drive from the contralesional to the ipsilesional M1 both at rest and immediately preceding movements of the paretic hand. Changes in premovement interhemispheric inhibition showed a trend for correlation with improvements in finger-tapping speed in the paretic hand.

Conclusion—The findings suggest that modulation of interhemispheric inhibitory interactions between the contralesional and ipsilesional M1, either primarily or secondary to intrahemispheric excitability changes in either hemisphere, may contribute to performance improvements with cutaneous anesthesia of the intact hand. The present study provides additional insight into the mechanisms by which rehabilitative interventions focused on training one hand and restraining the other may operate after chronic stroke.

Keywords

Anesthesia; Interhemispheric inhibition; Neurorehabilitation; Motor; Stroke

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Floel A, Hummel F, Duque J, Knecht S, Cohen LG. Influence of somatosensory input on interhemispheric interactions in patients with chronic stroke. *Neurorehabil Neural Repair*. 2008;22:477-485.

None of the authors reports any potential conflict of interest.

In recent years, there has been an increasing interest in understanding the mechanisms of human cortical plasticity that could support beneficial effects of customarily used neurorehabilitative treatments after stroke.^{1,3} So far, few interventional strategies have been tested, and none has reached universal acceptance as adjuvant treatments to physical therapy in the clinic.⁴

Intracortical excitatory and inhibitory activity changes in the ipsilesional and contralesional primary motor cortices (M1) after stroke.^{3,5} Interhemispheric inhibition from the contralesional to the ipsilesional M1 in patients with chronic subcortical stroke appears to be more persistent than in controls, particularly when patients move the paretic hand.^{6,7} Some of these abnormalities were more apparent when patients intended to move the paretic hand than when they were tested at rest.⁸ Using a paired pulse technique previously described,⁹ these studies demonstrated persistent inhibitory effects of a conditioning transcranial magnetic stimulation (TMS) pulse delivered to the contralesional M1 on motor-evoked potential (MEP) amplitudes in the paretic hand elicited by a TMS pulse applied to the ipsilesional M1. Support for a functional role of interhemispheric interactions on motor control¹⁰ comes from studies demonstrating the influence of activity of each M1 on motor performance in the ipsilateral hand¹¹ in healthy subjects and from the finding of performance improvements in paretic hand function elicited when decreasing excitability in the contralesional M1^{12,13} or when increasing excitability in the ipsilesional M1.^{14,15}

The purpose of this study was to evaluate IHI from the contralesional to the ipsilesional M1 before, during, and after intact hand (target intervention) and intact foot (control intervention) anesthesia in patients with chronic stroke to look for a possible link between performance improvements in paretic hand function and changes in IHI. The main finding was that premovement IHI from the contralesional to the ipsilesional M1 decreased proportionally to the improvements in finger-tapping speed in the paretic hand with intact hand anesthesia.

METHODS

Subjects

Ten chronic stroke patients with a single ischemic cerebral infarct (7 subcortical; 3 cortico-subcortical, not including primary motor cortex; Table 1; 35-85 years old, 62 ± 16 years; 4 of them women, all but 2 right-handed) gave informed consent to participate in the study. They were tested at least 1 year after the stroke (mean 4.5 ± 2.5 years; range, 1.5-7 years; Table 1). Patients included in the study (1) were not taking any medication that affects the central nervous system (eg, antipsychotics, antidepressants, or drugs affecting the dopaminergic system); (2) had normal routine medical and neurological examinations, except residuals of a single subcortical or cortical stroke (Table 1) with an initial severe hemiparesis (Medical Research Council [MRC] scale <2 ¹⁶) that had recovered to a degree so that they were able to perform the experimental tasks (MRC scale 3.8-4.9; see Table 1); (3) had no signs of dementia (Mini-Mental State Examination [MMSE] ≥ 27); and (4) were 18 to 80 years old.

The degree of spasticity was assessed with the modified Ashworth scale¹⁷ (see Table 1) and hand and arm function with the upper-extremity section of the Fugl-Meyer scale.¹⁸

Experimental Design (Figure 1)

After familiarization, patients participated in 2 different experimental sessions in a counterbalanced design in which they underwent ischemic anesthesia of the intact upper (target intervention) or lower (control intervention) extremity. In each session, testing of motor function (finger tapping) and electrophysiological measurements (motor threshold at rest, interhemispheric inhibition at rest [IHI_{REST}], and interhemispheric inhibition at about or immediately preceding movement onset [IHI_{MOVE}]) were evaluated. First, baseline determinations for each outcome measure (motor threshold, MEP amplitude, finger-tapping speed, and IHI_{REST} and IHI_{MOVE}) were taken. Cutaneous anesthesia was subsequently implemented in each session by inflation of a blood pressure cuff around the healthy wrist or healthy ankle above systolic blood pressure, for up to 50 minutes. A second measurement was done once during the anesthesia procedure, at a time when perception of light touch in the intact hand or foot (see below for details) was abolished. A third measurement was obtained 20 minutes after cuff release, at a time when sensation from the hand recovered. The second study day proceeded in identical order, with the only difference being the site of anesthesia (hand or foot). The limited number of neurophysiological evaluations allowed by the relatively short duration of the effects of cutaneous anesthesia was focused on repetitive evaluation of resting and premovement IHI, our primary endpoint measures.

Cutaneous Anesthesia

Anesthesia was achieved by inducing ischemic nerve block at the healthy wrist and ankle in separate sessions.^{19,21} The experimenter elevated the patient's arm or leg for 3 minutes to drain venous blood. A conventional sphygmomanometer, 7.5 cm wide, was placed at the wrist or the ankle and inflated to 40 mm Hg above systolic blood pressure. The arm or leg was then returned to the horizontal position. Low-threshold mechanoreceptive function (perception thresholds to light touch) at the distal pad of the second finger or toe was assessed using von Frey filaments (Aesthesiometer, Stoelting Co, Wood Dale, Illinois). Measurement of motor tasks started immediately after cutaneous anesthesia (defined at the time when light-touch perception was tested with a 4.56-mm diameter von Frey filament, which causes a visible skin indentation; target force 4 N; >50 times upper threshold limit was abolished in 5 of 5 successive trials). Mean duration of the anesthetic procedure was 45.5 ± 3.6 minutes for the hand and 46.5 ± 2.7 minutes for the foot. Subjects' perception of fatigue, attention to the task, and discomfort (questionnaires = Q in Figure 1A) were documented before and after each measurement and after cuff release, using visual analog scales that have good internal consistency, reliability, and objectivity.^{22,25}

Experimental Protocol

Finger-tapping task (Figure 1B)—Patients were seated in front of a conventional keyboard in an upright position with the forearm supported by a cushion. They were instructed to press a specific key with the paretic index finger as quickly as possible for a total of 10 seconds^{21,26,27} 3 times. Fifty seconds separated the 3 repetitions of this task,

which engages actively the primary motor cortex.^{21,28,30} The keyboard was connected to a laboratory computer that recorded the tapping interval (in ms), using Superlab Software (Cedrus Corporation, Palo Alto, California).

Reaction time measurements (Figure 1C)—Each subject sat in an armchair in front of a computer screen with his or her neck and arms comfortably supported by pillows.

Motor-evoked potentials were always recorded from the paretic hand. Before the experiment, subjects performed practice trials to familiarize themselves with the task, environment, and procedure. These trials were later used to characterize each individual's reaction time (RT) in the absence of TMS. RT was defined as the time between the GO signal and the onset of the electromyographic (EMG) response (at the time when it first exceeded 100 μ V peak to peak). Surface EMG was recorded from the first dorsal interosseus (FDI) muscle of both hands in a time window that comprised 500 ms before and 1000 ms after the test stimulus (TS; see below). After amplification and band-pass filtering (50–2000 Hz) using a Counterpoint Electromyograph (Dantec Electronics, Skovlunde, Denmark), the signal was digitized (sampling rate 5000 Hz) and stored on a personal computer for offline analysis using a data acquisition analysis system written in LabView.³¹ Trials with mirror or background EMG activity were excluded from analysis.

Measurement of IHI at rest—TMS was delivered from 2 Magstim 200 magnetic stimulators (Magstim, Whitland, Dyfed, UK), each connected to a figure-8 coil. The magnetic coil for the TS was positioned tangentially over the scalp with the handle pointing backward and perpendicular to the presumed direction of the central sulcus, about 45 degrees relative to the midsagittal line.³² The magnetic coil for the conditioning TMS pulse (CS) was oriented at 90 degrees relative to the midsagittal line, a position thought to elicit predominantly D³² and I₁ waves.³³ The optimal scalp position for eliciting a contralateral MEP was then identified and marked on a head cap placed on the subject's scalp. Resting motor threshold (rMT) was determined at this site and defined as the minimum stimulus intensity that produced MEPs $\geq 50 \mu$ V peak to peak in at least 5 of 10 trials.³⁴

For IHI_{REST} determination, a conditioning TMS pulse (CS) was applied to the contralesional M1, followed 10 ms later by a TS delivered to the ipsilesional M1. Trials using double pulses (CS and TS) were randomly intermixed with those using TS alone (Figure 2B). EMG responses were always recorded from the paretic hand contralateral to the TS stimulus. IHI was calculated as the amplitude of the conditioned MEPs in the double-pulse trials “CS and TS” relative to the amplitude of the test MEP when TS was delivered alone (CS and TS/TS). In this way, we measured IHI targeting the paretic hand (CS delivered to the contralesional M1 and TS delivered to ipsilesional M₁).

Specifically, for TS, we used the intensity of stimulation required to evoke MEP amplitudes of about 0.5 to 1.5 mV at rest,^{8,9} and for CS, we used the intensity required to evoke IHI of approximately 50% in CS and TS trials at rest.⁶ Patients with high rMT in whom these criteria could not be fulfilled were excluded from the study. A total of 20 CS and TS trials and 20 TS trials were acquired for each determination in each session. Single-pulse MEP

amplitudes recorded during determination of IHI_{REST} were analyzed separately to assess changes in overall cortical excitability with hand and foot anesthesia.

Measurement of movement-related IHI—In addition to measurements at rest, IHI was also measured in the process of generating a voluntary movement by the paretic hand in a simple RT paradigm (IHI_{MOVE}).⁶ The first IHI determination fell between 130 and 180 ms after the visual GO signal (between 40 and 60 ms before the RT measured in unstimulated trials), and the second IHI determination fell between 155 and 210 ms after the visual GO signal (between 20 and 30 ms before the RT measured in unstimulated trials). Because RT varies across subjects and IHI was determined at regular timings, the time interval between IHI determinations differed slightly across subjects, ranging from 20 to 30 ms. At each timing, 20 CS and TS trials and 20 TS-alone trials were presented in randomized order and with varying intertrial intervals (6-8 seconds) and organized into 5 experimental blocks. Because the focus of our interest was to characterize IHI before movement onset, at a time when the electrophysiological responses are not contaminated by motor activity, trials in which stimulation fell after EMG onset were excluded from analysis.⁶ This approach offers a cleaner reflection of premovement IHI than simply using all trials in the time interval immediately preceding the mean RT in unstimulated trials. For normalization purposes during IHI_{MOVE} , we chose parameters of TMS that resulted in comparable IHI at rest across subjects at baseline. Two subjects had to be excluded due to technical difficulties during determination of IHI_{MOVE} .

Statistical Analysis

Data analysis was performed by an investigator blind to the intervention type. Normal distribution (Shapiro-Wilk's test of normality) and homogeneity of variance (Bartlett's chi-square) were assessed for all data. Two patients had to be excluded from the analysis due to technical difficulties. To compare the effects of TIME (5 Q measurements, Figure 1A) and SITE of anesthesia (hand, foot) on the questionnaire measurements of fatigue, attention to task, and discomfort, we used separate ANOVA_{RM}, with TIME and SITE as the repeated measures. Similarly, separate ANOVA_{RM}, with TIME and SITE as the repeated measure were used to compare the effects of TIME (3 measurements; arrows in Figure 1A) and SITE of anesthesia (hand, foot) on finger-tapping intervals, motor thresholds, IHI_{REST} , and IHI_{MOVE} . Conditioned on significant F values ($P < .05$), appropriate post hoc analyses were conducted. A simple regression analysis was conducted to assess the association between the independent variable “decrease in IHI_{MOVE} ” and “improvement in finger-tapping intervals” during hand anesthesia. All data are expressed as mean $\pm$ SEM.

RESULTS

Psychophysical Assessments (Table 2)

ANOVA_{RM} for fatigue, attention, and discomfort showed a significant effect of TIME ($F_{(1, 18)} = 3.2$, $P = .02$ for fatigue; $F_{(1, 18)} = 1.02$, $P = .4$ for attention; $F_{(1, 18)} = 31.1$, $P < .0001$ for discomfort; and $F_{(1, 18)} = 125$, $P < .0001$ for light-touch perception in the intact hand) but not SITE of anesthesia or TIME $\times$ SITE of anesthesia interaction (all $F_{(4, 72)} < 2.1$, $P > .09$), reflecting an increment in discomfort and fatigue and a decrement in attention over

time that was comparable with hand and foot anesthesia (Table 2). Discomfort remitted completely after cuff deflation. No significant effects emerged for the Modified Ashworth Spasticity Scale.

Motor Performance

ANOVA_{RM} showed a significant TIME $\times$ SITE of anesthesia interaction on finger-tapping intervals expressed as a percentage of baseline values, $F_{(2, 28)} = 4.1$, $P = .027$. Post hoc testing showed a significant reduction of finger-tapping intervals in the paretic hand, reflecting faster speed performance, during anesthesia of the intact hand ($P < .05$) but not with anesthesia of the intact foot. A trend for shortening in tapping intervals remained present at the measurement performed 20 minutes after the end of the anaesthetic procedure but did no longer reach significance.

Motor Thresholds

Motor thresholds were comparable in each session before and after anesthesia (Table 3), in line with previous studies.^{19,20} Although there was a trend for higher motor threshold in the ipsilesional compared with the contralesional M1, the difference did not reach significance.

Interhemispheric Inhibition at Rest

Baseline IHI_{REST} did not differ significantly in the 2 sessions (hand anesthesia: 0.81 ± 0.13 ; foot anesthesia: 0.82 ± 0.08). Hand anesthesia turned IHI_{REST} into facilitation (to 1.12 ± 0.09 during and 1.18 ± 0.2 post), but no significant changes were identified with leg anesthesia (to 0.87 ± 0.05 during and 0.78 ± 0.05 post). ANOVA_{RM} for IHI_{REST} (SITE $\times$ TIME) showed a significant TIME $\times$ SITE of anesthesia interaction, $F_{(2, 28)} = 6.4$, $P = .0052$. Post hoc testing showed a significant change of IHI_{REST} to facilitation during and after hand anesthesia but not with foot anesthesia.

Movement-Related Interhemispheric Inhibition

Baseline IHI_{MOVE} did not differ significantly across sessions (0.81 for hand and 0.83 for leg anesthesia) and did not show the characteristic premovement modulation previously described in healthy volunteers.^{6,7} ANOVA_{RM} for IHI_{MOVE} showed a significant TIME $\times$ SITE of anesthesia interaction, $F_{(2, 28)} = 3.4$, $P = .046$. Post hoc testing revealed that hand anesthesia reduced the inhibitory drive from the contralesional to the ipsilesional M1 present with movements of the paretic hand, both during and 20 minutes after cuff deflation (Figure 2A). The magnitude of this reduction showed a trend for correlation with the magnitude of speed performance improvements in finger-tapping intervals, $R^2 = 0.45$, $F_{(1, 7)} = 5.07$, $P = .065$ (Figure 3). No changes were identified during leg anesthesia.

Motor-Evoked Potentials

Motor-evoked potential amplitudes in the paretic hand showed a nonsignificant trend to increase from 1.04 ± 0.23 mV at baseline to 1.14 ± 0.25 during and 1.3 ± 0.28 after hand anesthesia, $F_{(1, 9)} = 2.75$, $P = .14$, *ns*. With foot anesthesia, MEP amplitudes decreased slightly from 1.17 ± 0.16 mV at baseline to 1.15 ± 0.4 and 1.02 ± 0.5 mV after, respectively (also *ns*).

DISCUSSION

The main finding of this study was that cutaneous anesthesia of the intact hand in patients with chronic, predominantly subcortical stroke resulted in reduction of the inhibitory drive from the contralesional to the ipsilesional M1 both at rest and immediately preceding movements of the paretic hand. The magnitude of paretic hand improvement showed a trend for correlation with the reduction in IHI_{MOVE} .

Effects of cutaneous anesthesia of the intact hand on motor function in the paretic hand after stroke

Reduction of somatosensory input by cutaneous anesthesia of the intact hand results in improvements in motor performance^{21,35} and in tactile discriminative skills in the paretic hand after stroke.³⁶ In healthy humans, cutaneous anesthesia of one hand leads to performance improvements in the opposite hand,³⁷ a phenomenon accompanied by modulation of interhemispheric inhibition.¹⁹ The similar finding reported here in patients with stroke is consistent with one of the proposed beneficial influences of immobilization of the intact hand (which reduces somatosensory input from the immobilized limb) on training-dependent motor improvements in the paretic hand during constraint-induced (CI) movement therapy³⁸ but may not be as important as the intensity of task practice of the affected one.³⁹ Therefore, the beneficial influence of reducing somato-sensory input from one limb on motor performance in the opposite limb has been documented across laboratories in both animal models and in humans with and without brain lesions. The behavioral gains in paretic hand function after cutaneous anesthesia in our study were consistent qualitatively and quantitatively with those identified in previous investigations in patients with stroke.²¹

In terms of underlying mechanisms, reduction of sensory input from one limb elicits bilateral cortical reorganization characterized by rapid changes in receptive fields in the somatosensory cortex in animal models.⁴⁰ It has been proposed that these changes could be mediated through modulation of interhemispheric inhibitory mechanisms²¹ comparable to those operating in other sensory systems.^{10,37} The present investigation intended to gain information on this hypothesis.

Effects of cutaneous anesthesia on interhemispheric inhibitory interactions—

The novel finding of this study was that cutaneous anesthesia of the intact hand reduced the inhibitory drive from the contralesional to the ipsilesional M1 both at rest and in the premovement stage and that the changes in premovement showed a trend for correlation with the shortening in finger-tapping intervals (a reflection of tapping speed). What particular mechanisms could explain these changes? Interhemispheric inhibition, as tested with the paired pulse technique, is mediated through transcallosal glutamatergic excitatory fibers, which synapse with GABAergic interneurons that target pyramidal tract neurons in the opposite hemisphere.^{9,41} The net physiological effect when the intervals between conditioning and test pulses are shorter than 100 ms is predominantly inhibitory¹¹ at rest but may become excitatory,⁹ particularly when testing is done close to movement onset¹¹ as, for example, in reaction time paradigms.⁴² Theoretically, changes in interhemispheric

interactions could be induced through modulation of excitability in glutamatergic transcallosal pathways or through excitability changes in each of the hemispheres.^{43,45} Intrahemispheric excitability changes do occur with cutaneous anesthesia, which induces a decrease in cortical excitability of the deafferented body part representation in the M1 contralateral to the anesthetized hand²⁰ and an increase in excitability in the M1 ipsilateral to the anesthetized hand.¹⁹ In addition, multiple other intracortical mechanisms could modulate activity in each M1 and could secondarily influence IHI measurements both at rest and in the premovement period, including short intracortical inhibition (ICI⁴⁶), long ICI,⁴⁷ afferent feedback,⁴⁸ intracortical facilitation,⁴⁹ cerebello-cortical,⁵⁰ posterior parietal cortex-M1,⁵¹ supplementary motor area-M1,⁵² and dorsal premotor cortex-M1⁵³ interactions. One possibility is that performance improvements in the paretic hand identified in our study could benefit from an overall reduction of the inhibitory drive from the contralesional to the ipsilesional M1 reached through changes in one or in a combination of these various mechanisms. Because of the limited duration of the effects of cutaneous anesthesia, we could not evaluate all these physiological mechanisms in this particular experimental paradigm in stroke patients. Such detailed investigation on the influence of all these different mechanisms on IHI has not been done yet in healthy subjects either.

One methodological consideration is that, although we marked the coil position with a pen on the cap and ascertained the TMS coil position repeatedly during the experiment, minor displacements resulting in increased intertrial variability of CS or TS MEP amplitudes before, during, and after both hand and foot anesthesia procedures cannot be completely ruled out. Even if present, such effect could not explain the differential effects of hand and foot anesthesia reported here.

Another methodological consideration is that, during anesthesia, the magnitude of MEPs elicited in muscles below the anesthetic cuff are known to decrease and disappear at the time of motor block (see, for example, Werhahn et al¹⁹ and Ziemann et al²⁰). However, in addition to this progressive decrease in MEP amplitude below the anesthetic cuff, it has been shown that descendent efferent volleys elicited by a TMS stimulus over the deafferented hemisphere targeting the deafferented body part increase.⁵⁴ Therefore, a CS TMS stimulus over the deafferented hemisphere elicits more prominent descending output during anesthesia.⁵⁴ We decided, on the basis of this evidence, to avoid adjusting the CS TMS intensity, therefore biasing against our experimental hypothesis, which predicted a decrease in IHI (facilitated by a hypothetical correction of CS stimulus intensities). Our estimate of the modulatory effect of intact hand anesthesia on IHI from the intact to the affected motor cortex is likely to be, under these circumstances, rather conservative.

In summary, our findings support the view that performance improvements in paretic hand function with cutaneous anesthesia of the intact hand may relate partially to changes in interhemispheric inhibitory interactions from the contralesional to the ipsilesional M1. The hypothesis tested in this article provides additional insight into the mechanisms by which rehabilitative interventions focused on training one hand and restraining the other operate after chronic stroke.

ACKNOWLEDGMENTS

We thank S. Ravindran for help with patient recruitment, N. Dang for providing technical help, and C. Breitenstein for helpful discussions on the manuscript.

This work was supported by the intramural research program of the National Institute of Neurological Disorders and Stroke, the Deutsche Forschungsgemeinschaft to AF (FI 379-1/1, FI 379-4/1), the Bundesministerium for Bildung und Forschung to AF (01GW0520, part 4), the Nordrhein-Westfalen Ministry of Education and Research to AF (Lise Meitner Stipendium), and the Innovative Medizinische Forschung Münster to AF (FL110605).

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Figure 1.

Experimental design. (A) Time course of the experiments. Measurement of finger-tapping task and spasticity in the paretic hand, light-touch perception in the intact hand, IHI_{REST} and IHI_{MOVE} (black arrows), and assessment of fatigue, attention to the task, and discomfort (Q1 through Q5) before, during, and after anesthesia of the intact hand/leg. The same experimental timeline was implemented in both experimental sessions (intact hand and intact leg anesthesia). (B) Measurements of finger-tapping task. Patients were instructed to press a specific key on a conventional keyboard as fast as possible for a total of 10 seconds. (C) Measurement of interhemispheric inhibition (IHI) from the contralesional to the ipsilesional M1. IHI was evaluated at rest (IHI_{REST}) and in the process of generating a voluntary movement in a simple reaction time (RT) paradigm (IHI_{MOVE}) according to previously described protocols. For IHI_{MOVE} , subjects responded with a fast voluntary index finger movement in the paretic hand to a visual GO signal (right). The onset of the electromyogram (EMG) response recorded from the paretic first dorsal interosseus (FDI) muscle (diagram shown in the left) characterized the RT. IHI_{MOVE} was studied by delivering a conditioning stimulus (CS) to the contralesional M1 (shown off the head for clarity in C) and a test stimulus (TS) to the ipsilesional M1.⁶ Motor-evoked potentials (MEPs) were recorded from the paretic hand contralateral to the TS. IHI was measured at 2 different timings preceding the RT. Two different transcranial magnetic stimulation (TMS) coils were used for CS and TS.

Figure 2.

Interhemispheric inhibition (IHI) from contralesional to ipsilesional M1. (A) Group data. The y-axis shows IHI_{MOVE} targeting the paretic hand in the 2 experimental sessions (values under 100% note inhibition and above 100% facilitation). Note the clear attenuation of IHI_{MOVE} (approaching 100%) during and up to 20 minutes after cutaneous anesthesia of the intact hand (white bars). (B) Representative examples of motor-evoked potential (MEP) recorded from the paretic hand (first dorsal interosseus) in the reaction time paradigm before (pre) and during (anesthesia) cutaneous anesthesia of the intact hand. Upper insets show test MEP at the 2 time points of the experiment. Lower insets show conditioned MEP. Note the comparable test MEP amplitudes in the paretic hand pre and during anesthesia of the intact hand periods (upper insets). The addition of the CS (lower insets) elicited substantial inhibition of the MEP amplitude in the “pre” period (compare left lower with left upper inset). During anesthesia of the intact hand, the CS failed to elicit inhibition of the MEP amplitude in the paretic hand (compare right lower with upper inset). SA, stimulus artefact; RT, reaction time; TS, test stimulus; CS, conditioning stimulus; IHI_{MOVE}, CS and TS/TS.

Figure 3.

Improvements in finger-tapping speed in the paretic hand elicited by cutaneous anesthesia of the intact hand were more prominent (trend) in patients who experienced a more prominent attenuation of IHI_{MOVE}. IHI, interhemispheric inhibition.

Table 1

Clinical Characteristics of Stroke Patients

Patient	Age	Sex	Years Poststroke	Lesion Site	Motor Function		
					MRC	FMS, %	MAS
1	79	M	5	R-centrum semiovale	4.4	94	1+
2	63	F	6	L-fronto-parietal cortex, corona radiata	3.8	82	3
3	40	M	7	R-frontal operculum, putamen, corona radiata, and insula	4.8	95	2
4	85	M	9	L-basal ganglia	4.8	96	0
5	65	F	12.5	R-basal ganglia, centrum semiovale, corona radiata	4.5	85	1+
6	70	M	2	L-occipito-posterior junction centrum semiovale	4.7	91	1+
7	65	M	2	R-thalamus	4.9	95	0
8	63	F	1.5	R-temporal lobe, R-centrum semiovale	4.5	92	0
9	35	F	5	R-putamen and corona radiata	4.0	85	1
10	53	M	2	L-insula, inferior parietal lobule, frontal lobe	4	81	2

F, female; M, male; L, left hemisphere; R, right hemisphere; MRC, Medical Research Council scale⁵⁵; FMS, Fugl-Meyer Scale¹⁸; MAS, Modified Ashworth Scale¹⁷ for rating spasticity.

Table 2

Discomfort, Attention, Fatigue, Perception of Light Touch, and Spasticity

Measurement Group	Pre	Anesthesia			Post	
		1	2	3		
Intact hand anesthesia	Discomfort	1 ± 0	3.8 ± 0.9	1.4 ± 0.4	4.1 ± 0.8	4.7 ± 0.9
	Fatigue	8.1 ± 0.9	6.7 ± 0.8	7.3 ± 0.8	6.7 ± 0.8	6.5 ± 0.8
	Attention	7.6 ± 0.8	6.6 ± 0.8	6.8 ± 0.7	6.5 ± 0.7	6.3 ± 0.7
	MF	5 ± 0	3.9 ± 0.6	5 ± 0	1.3 ± 0.5	0
	MAS	0.95 ± 0.3	0.85 ± 0.3	0.95 ± 0.2	0.7 ± 0.3	0.95 ± 0.2
Intact leg anesthesia	Discomfort	1 ± 0	3.2 ± 0.6	1 ± 0	4.7 ± 0.6	5.3 ± 0.7
	Fatigue	7.1 ± 0.7	7.5 ± 0.8	7.3 ± 0.7	7.1 ± 0.7	6.5 ± 0.8
	Attention	7.1 ± 0.7	6.9 ± 0.6	6.8 ± 0.6	6.8 ± 0.6	6.2 ± 0.6
	MF	5 ± 0	5 ± 0	5 ± 0	1 ± 0.6	0
	MAS	1 ± 0.3	0.8 ± 0.3	0.8 ± 0.3	1 ± 0.3	0.8 ± 0.3

Pre, assessment before anesthesia; 1, first assessment during anesthesia; 2, second assessment during anesthesia; 3, third assessment during anesthesia, before IHIREST and IHIMOVE; Post, assessment 5 minutes after cuff release; MF, low-threshold mechanoreceptive function

(perception thresholds to light touch); MAS, Modified Ashworth Scale¹⁷ for rating spasticity. Discomfort, attention, and fatigue were self-assessed by the subjects using visual analog scales (1 = lowest and 10 = highest). Note that discomfort and fatigue increased progressively over time with both interventions, whereas self-reports of attention decreased over time to a comparable extent with both interventions. Perception to light touch in the anesthetized limb decreased progressively over the course of the experiment and was abolished before the measurement of IHIREST and IHIMOVE. Spasticity did not change significantly.

Table 3

Motor Thresholds (% of Maximal Stimulator's Output)

	MT _{CL M1 pre} , %	MT _{IL M1 pre} , %	MT _{IL M1 anesthesia} , %
Hand anesthesia	44.9 ± 5.4	47 ± 4.7	46.2 ± 4.7
Foot anesthesia	44.4 ± 5.6	48.5 ± 5.6	48.8 ± 5.8

MT in contralesional M1 before anesthesia (MT_{CL M1 pre}). MT in ipsilesional M1 before (MT_{IL M1 pre}) and after (MT_{IL M1 anesthesia}) cutaneous anesthesia of intact hand and leg.