Influence of Somatosensory Input on Motor Function in Patients with Chronic Stroke

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In healthy volunteers, reduction of somatosensory input from one hand leads to rapid performance improvements in the other hand. Thus, it is possible that reduction of somatosensory input from the healthy hand can influence motor function in the paretic hand of chronic stroke patients with unilateral hand weakness. To test this hypothesis, we had 13 chronic stroke patients perform motor tasks with the paretic hand and arm during cutaneous anesthesia of the healthy hand and healthy foot in separate sessions. Performance of a finger tapping task, but not a wrist flexion task, improved significantly with anesthesia of the hand, but not the foot. This effect progressed with the duration of anesthesia and correlated with baseline motor function. We conclude that cutaneous anesthesia of the healthy hand elicits transient site-specific improvements in motor performance of the moderately paretic hand in patients with chronic stroke, consistent with interhemispheric competition models of sensorimotor processing.

Stroke is the third leading cause of death and the leading cause of adult disability in the United States.[1] Although mortality has declined, two thirds of stroke survivors have residual neurological deficits.[2] Motor disability reduces functional independence by compromising activities of daily living, such as dressing, bathing, engaging in self-care, and writing,[3] in the absence of universally accepted treatments for this condition.[4]

It has been proposed that application of principles of neuroplasticity identified in animal models[5] could improve chronic motor disability resulting from stroke.[4] Recent reports of studies in flying fox and primates have noted that reduction of sensory input from one limb results in bilateral cortical reorganization characterized by rapid changes in receptive fields in the somatosensory cortex.[6] In humans, hand anesthesia also leads to bilateral cortical reorganization[7, 8] and, interestingly, to improvements in tactile discriminative skills in the nonanesthetized hand,[9] possibly through modulation of interhemispheric interactions.[7] It is conceivable, then, that anesthetizing the healthy hand of chronic stroke patients could influence motor function in the paretic hand. In this study, we evaluated the effects of cutaneous anesthesia of the healthy hand and healthy foot (control) on performance of a finger tapping task and a forearm motor task implemented by the paretic arm in patients with chronic stroke.

Subjects and Methods

Thirteen patients aged 63.8 ± 4.6 years (six of them females, all but two were right-handed) with cerebral infarcts participated in the study. All participants had a single ischemic cerebral infarct (11 subcortical; 2 corticosubcortical, not including primary motor cortex; Table 1). All gave written informed consent to each experiment according to the Declaration of Helsinki (http://www.wma.net/e/policy/17-c_e.html)[10] and the National Institute of Neurological Disorders and Stroke Institutional Review Board approved the study protocol. Patients were tested at least 1 year after the stroke (6.5 ± 1 year after the ictal event; range, 2.7–13.3 years; see Table 1). All patients initially had a severe motor paresis (below Medical Research Council [MRC] scale[11] grade 2) and recovered substantially (range on MRC scale from 2.7 to 4.8; see Table 1) to be able to perform both motor tasks. Degree of spasticity was assessed with the modified Ashworth scale for grading spasticity (MAS)[12] and ranged from 0 to 3 (see Table 1); muscle strength was assessed with the upper extremity section of the Fugl-Meyer scale (FMS).[13] All patients had visual perception, somatosensory function, and Mini-Mental State Examination (range, 26–30 points) within normal limits, as tested during a regular neurological examination.

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Table 1. Clinical Characteristics of Stroke Patients

Patient No.	Age (yr)	Sex	Years after Stroke	Lesion Site	Motor Function		
					MRC	FMS	MAS
1	79	M	5	R-centrum semiovale	4.4	94%	1+
2	60	F	3	L-frontoparietal cortex, corona radiata	3.8	82%	3
3	66	M	8.6	L-internal capsule, centrum semiovale	4.4	87%	1+
4	74	M	8.7	R-parietal and temporal cortex, corona radiata, centrum semiovale, thalamus	4.7	88%	2 to 3
5	54	F	5.4	R-basal ganglia	3.0	76%	2
6	75	F	2.7	R-putamen and corona radiata	4.7	89%	2
7	60	M	3.3	L-basal ganglia	4.5	79%	3
8	35	M	3.6	R-frontal operculum, putamen, corona radiata, and insula	4.8	95%	2
9	76	F	13.3	L-internal capsule to centrum semiovale	4.0	83%	1+
10	23	M	4.3	R-medial temporal lobe, basal ganglia, corona radiata	3.5	76%	2
11	71	F	6.5	L-corona radiata	2.7	53%	3
12	83	M	7.5	L-basal ganglia	4.8	96%	0
13	65	F	12.5	R-basal ganglia, centrum semiovale, corona radiata	4.5	85%	1+ to 2
X ± SEM	63.8 ± 4.6		6.5 ± 1		4.1 ± 0.2	83 ± 3.1	1.96 ± 0.2

L = left hemisphere; R = right hemisphere; MRC = Medical Research Council scale[10]; FMS = Fugl-Meyer scale[13]; MAS = modified Ashworth scale[12] for rating spasticity; SEM = standard error of the mean.

Experimental Design

The finger-tapping and wrist-flexion tasks were evaluated on three different days, as follows: (a) practice session in the absence of anesthesia, (b) anesthesia of the healthy hand (target intervention), and (c) anesthesia of the healthy foot (control intervention). Order of anesthesia sessions was counterbalanced among patients. On the first day, patients participated in a practice session and became familiar with the study requirements and the experimental tasks. Instructions and order of presentation of the tasks in each session were identical on each of the three days. Sessions b and c (anesthesia sessions) started with the determination of baseline measurements for each motor task. Cutaneous anesthesia then was implemented by inflation of a blood pressure cuff around the healthy wrist (session b) and healthy ankle (session c) above systolic blood pressure, for up to 48 minutes.[7,9,14–17] Motor tasks were measured twice during the anesthetic period. A fourth measurement was obtained 20 minutes after cuff release, at a time when sensation from the hand had been recovered.[7, 9,14–17] For consistency, instructions were played from a tape recorder, and no feedback on motor performance was provided at any time.

Anesthetic Procedure

Anesthesia was achieved by inducing ischemic nerve block at the healthy wrist and ankle in separate sessions. The experimenter elevated the patient's arm or leg for 3 minutes to drain venous blood. A conventional sphygmomanometer, 7.5cm wide, was placed at the wrist (session b) or the ankle (session c) and inflated to 40mm Hg above systolic blood pressure. The arm or leg then was 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, Wood Dale, IL). Complete anesthesia was defined at the time when light-touch perception tested with a 4.56mm-diameter von Frey filament (which causes a visible skin indentation; target force 4 N; > 50 times upper threshold limit) was abolished in five of five successive trials. Mean duration of the anesthetic procedure was 35.3 ± 4.3 minutes for the hand and 38.3 ± 4.1 minutes for the foot. Measurement of motor tasks started immediately after cuff inflation. Subjects' perception of fatigue, attention to the task, and pain (psychophysical assessments [PA]; Fig 1A) were documented before and after each of the four motor task measurements and immediately after cuff release using visual analog scales. Patients rated their level of fatigue (ranging from 1 to 7), their attention toward the task (ranging from 1 to 7), and the intensity and affective reaction to the cuff-induced discomfort (ranging from 1 to 7). These scales have good internal consistency, reliability, and objectivity.[18–21] (see Fig 1A).
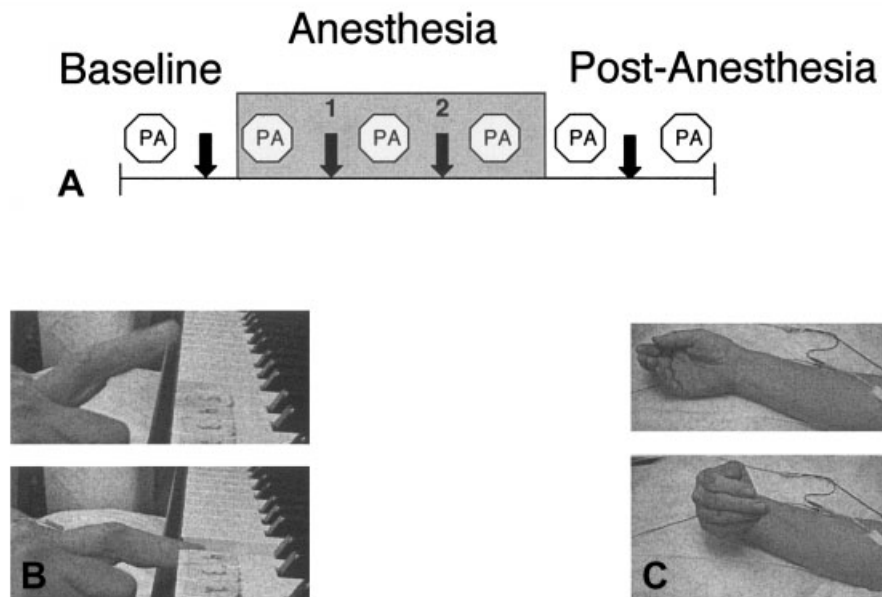
Fig 1. Experimental design. Time course of the experiments (A), including measurement of finger-tapping (B) and wrist-flexion (C) tasks by the paretic hand (arrows) and assessment of fatigue, attention to the task, and discomfort (psychophysical assessment [PA]) at different times before, during, and after anesthesia of the intact hand.

Finger-Tapping Task

Patients were seated in front of an electronic keyboard (Yamaha pf85; Yamaha, Hamamatsu Shizuoka, Japan) in an upright position with the forearm supported by a cushion (see Fig 1B). They were instructed to press a specific key with the paretic index finger as quickly and regularly as possible for a total of 10 seconds.[22] Fifty seconds separated the three repetitions. The keyboard was connected to a laboratory computer that recorded the tapping interval (in milliseconds), tapping force exerted on the piano key (expressed on an arbitrary ordinal scale with values ranging from 1 to 127), and variability of tapping intervals (expressed as a coefficient of variance [standard deviation/mean] of the tapping interval), using Vision 1.4 (Opcode Systems, Palo Alto, CA). This task relies predominantly on activity originating in the primary motor cortex.[23–25]

Wrist-Flexion Task

Patients were seated 60cm in front of a 20-inch monitor with both arms supported by a cushion (see Fig 1C). Patients were instructed to focus on a cross in the center of the screen and to bend their wrists as quickly as possible in response to a GO signal presented on the monitor. Each trial started with a visual warning signal ("Get ready …"), followed at random intervals (2–6 seconds) by a GO signal. Each measurement consisted of 23 wrist-flexion trials (3 of them practice trials). Electromyogram (EMG) was recorded from silver-silver chloride electrodes positioned in a belly tendon montage on the skin overlying the flexor carpi radialis (50Hz to 2kHz, sampling rate 5kHz) from a Counterpoint Electromyograph (Dantec Electronics, Skovlunde, Denmark). The reaction time (in milliseconds) was defined as the time interval between the GO signal and the onset of the EMG burst in the flexor carpi radialis muscle.

Data Analysis

Data analysis was performed by an investigator blind to the intervention type. Normal distribution (Shapiro–Wilk test of normality) and homogeneity of variance (Bartlett's χ^2) were assessed for all data. To compare the effects of TIME (six PA measurements; see Fig 1A) and SITE of anesthesia (hand, foot) on the psychophysical measurements of fatigue, attention to task, and pain, we used separate ANOVA$_{RM}$, with TIME as the repeated measure and SITE as the within-subject factor. Similarly, separate ANOVA$_{RM}$, with TIME as the repeated measure and SITE as the within-subject factor, were used to compare the effects of TIME (four motor-task measurements; arrows in Fig 1A) and SITE of anesthesia (hand, foot) on tapping interval, tapping force, and variability of tapping intervals in the finger-tapping task and reaction time (RT) in the wrist-flexion task. Practice effects were evaluated using one-way ANOVA$_{RM}$, with TIME as the repeated measure (five determinations in the absence of anesthesia). Conditioned on significant F-values ($p < 0.05$), post hoc analyses were conducted using Tukey tests. Correlation between Fugl-Meyer score[13] and improvement in finger tapping during hand anesthesia was assessed with Spearman's rank correlation. All data are expressed as mean ± SEM.

Results

ANOVA$_{RM}$ for fatigue and attention did not show effects of TIME ($F_{(5,60)} = 0.54$, not significant [NS], and $F_{(5,60)} = 0.38$, NS, respectively), SITE of anesthesia ($F_{(1,12)} = 0.96$, NS, and $F_{(1,12)} = 0.95$, NS, respectively), or TIME × SITE of anesthesia interaction ($F_{(5,120)} = 0.91$, NS, and $F_{(5,120)} = 0.93$, NS, respectively). In contrast, ANOVA$_{RM}$ for pain showed significant effects of TIME ($F_{(5,60)} = 24.6$, $p < 0.01$), but

not SITE of anesthesia ($F_{(1,12)} = 1.5$, NS) or TIME × SITE of anesthesia interaction ($F_{(5,120)} = 1.5$, NS), reflecting a comparable increment in discomfort with hand and foot anesthesia that remitted completely after cuff deflation (Table 2). In the absence of anesthesia, repeated performance of the two motor tasks in the first session (see Subjects and Methods) did not result in changes in finger-tapping interval ($F_{(4,48)} = 2.32$, NS), finger-tapping force ($F_{(4,48)} = 0.54$, NS), finger-tapping interval variability ($F_{(4,48)} = 0.20$, NS), or wrist-flexion RT ($F_{(4,48)} = 0.45$, NS; Table 3).

Effects of Anesthesia of the Healthy Hand on Motor Performance of the Paretic Hand

FINGER-TAPPING TASK. ANOVA$_{RM}$ showed a significant TIME × SITE of anesthesia interaction on finger-tapping intervals expressed in milliseconds ($F_{(3,72)} = 2.8$, $p < 0.05$) and as percentage of baseline values ($F_{(3,72)} = 3.6$, $p < 0.05$; see Fig 2A). Post hoc testing showed a significant reduction of finger-tapping intervals in the paretic hand during anesthesia of the intact hand (first measurement: $p < 0.05$; second measurement: $p < 0.01$) but not with anesthesia of the intact foot (see Fig 2A). The shortening in tapping intervals remained present for at least 20 minutes after the end of the anesthetic procedure ($p < 0.05$) but returned to approximately 89% of baseline values (NS) 24 to 48 hours later.

Tapping force and variability showed a trend for increased tapping force and decreased variability of tapping intervals (first measurement: $p = 0.05$ and $p < 0.05$, respectively; second measurement: $p = 0.048$ and $p < 0.01$, respectively).

WRIST-FLEXION REACTION TIME. ANOVA$_{RM}$ did not show significant effects of TIME, SITE, or TIME × SITE of anesthesia interaction on wrist-flexion reaction times (see Fig 2B).

Relation between Improvements in Finger-Tapping Intervals and Motor Function

Patients were stratified according to motor strength (as assessed by the FMS) into a group with good (n = 7) and a group with poor (n = 6) motor function (median split of score in FMS). Improvement in finger-tapping intervals during hand anesthesia correlated well with Fugl-Meyer scores only in patients with better motor function ($r = 9.2$; $p < 0.01$; Fig 3).

Discussion

The main result of this study was that cutaneous anesthesia of the intact hand of chronic stroke patients resulted in improvements in performance of a dynamic finger motor task with the paretic hand.

Rapid finger tapping is a task that relies predominantly on activity originating in the primary motor cortex[23] and conducted through fast corticospinal projections.[26] It correlates well with the achievement of functional goals in patients with brain lesions undergoing rehabilitative treatments.[27,28] In this study, we found that cutaneous anesthesia of the healthy hand led to a significant improvement in tapping speed in the paretic hand that started rapidly after the onset of anesthesia, peaked at the end of the anesthetic procedure, and outlasted the anesthesia period by at least 20 minutes. The magnitude of this improvement (18%) was similar to improvements reported in performance of a different task with the same anesthetic procedure in healthy volunteers (19%).[9] The effect was topographically specific because (1) it was not found with anesthesia of the intact foot, which scored similarly to anesthesia of the intact hand in terms of discomfort, fatigue, and attentional load, and (2) anesthesia of the intact hand improved performance in the dynamic distal-finger motor task but not in the wrist-flexion task, which predominantly engages forearm muscles proximal to the anesthetic level (wrist).

Table 2. Fatigue, Attention to Task, and Pain Ratings

Measurement	Baseline[a]	Anesthesia			Postanesthesia	
		1	2	3	1	2
Hand anesthesia						
Fatigue	4.3 ± .0	4.3 ± .5	4.2 ± .72	4.3 ± .50	4.3 ± .72	4.5 ± .88
Attention	4.8 ± .6	4.5 ± .5	4.2 ± .84	4.3 ± .71	4.4 ± .71	4.7 ± .63
Pain	1.0 ± 0	2.1 ± 1.2	3.7 ± 1.1	4.0 ± 1.3	2.3 ± 1.0	1.0 ± .00
Foot anesthesia						
Fatigue	4.5 ± .1	4.3 ± .7	4.2 ± 1.1	4.3 ± .75	4.3 ± .79	4.3 ± .69
Attention	4.8 ± .6	4.6 ± .7	4.6 ± 1.2	4.6 ± .77	4.5 ± .79	4.6 ± .71
Pain	1.0 ± 0	2.4 ± 1	3.0 ± .87	3.3 ± 1.1	1.9 ± 1.0	1.0 ± .00

[a]Baseline measurement; 1: first measurement during anesthesia; 2: second measurement during anesthesia; 3: third measurement during anesthesia, before cuff release; after anesthesia 1: measurement 5 minutes after cuff release; after anesthesia 2: measurement 20 minutes after cuff release.

Table 3. Performance in Repeated Sessions in the Absence of Anesthesia

Test	Day 1 (practice day)			Day 2 (anesthesia), Baseline day 2	Day 3 (anesthesia), Baseline day 3
	Practice 1	Practice 2	Practice 3		
Tapping interval(s)	0.76 ± 0.16	1.03 ± 0.18	0.76 ± 0.10	0.84 ± 0.15	0.86 ± 0.14
Tapping force (0–127)	57.2 ± 5.4	58.5 ± 5.0	57.3 ± 5.6	58.8 ± 5.3	60.4 ± 6.6
Variability	0.38 ± 0.007	0.42 ± 0.1	0.42 ± 0.06	0.38 ± 0.11	0.43 ± 0.1
Reaction time (msec)	302 ± 18.2	303 ± 14.4	303 ± 12.2	294 ± 8.4	289 ± 12.3

Tapping force: force exerted on piano key, expressed on an arbitrary scale from 0–127; variability: variability of tapping intervals, measured as the coefficient of variation of the tapping interval (Cv = standard deviation/mean); Practice 1–3: three practice measurements on first study day; Baseline days 2 and 3: baseline measurements on days 2 and 3 (anesthesia sessions), respectively.

Somatosensory input is required for accurate motor performance[29] and for motor skill acquisition.[30] Reduction of such input by local anesthesia impairs motor control,[31,32] as shown in patients with large-fiber sensory neuropathy who display characteristically abnormal motor behavior.[33,34] In patients with stroke, somatosensory deficits are associated with slower recovery of motor function.[35] Given the existence of physiologically active interhemispheric interactions between motor and sensory cortices,[7,36–44] it is not surprising that somatosensory input from one hand could influence motor function in the other hand in the healthy central nervous system.[7] We have now applied this principle of neuroplasticity, demonstrated previously in healthy volunteers, to a group of chronic stroke patients, and documented an improvement of approximately 20% in a motor task performed by the paretic hand with anesthesia of the opposite, healthy hand. This finding supports the view that somatosensory input from the healthy hand influences motor control in the paretic hand. It is possible that modulation of somatosensory input originating in the intact hand, in combination with motor training of the paretic hand, could enhance the beneficial effects of training alone. Although the specific mechanisms underlying this effect remain to be determined, they could involve modulation of abnormal intracortical inhibition in the affected hemisphere[45] and/or a correction of abnor-
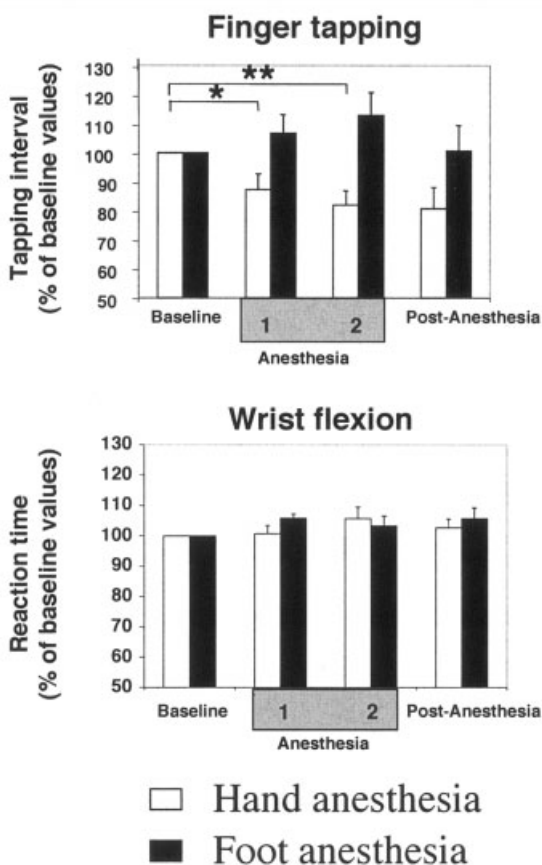

*Fig 2. Finger-tapping interval (A) and wrist-flexion reaction time (B) in the paretic hand during anesthesia of intact hand (white bars) and intact foot (black bars). Note that finger-tapping intervals were shorter during hand anesthesia, denoting improved performance that outlasted the period of anesthesia. In contrast, foot anesthesia resulted in a trend for longer tapping intervals. Neither hand nor foot anesthesia significantly influenced wrist-flexion reaction times. *p < 0.05; **p < 0.01.*
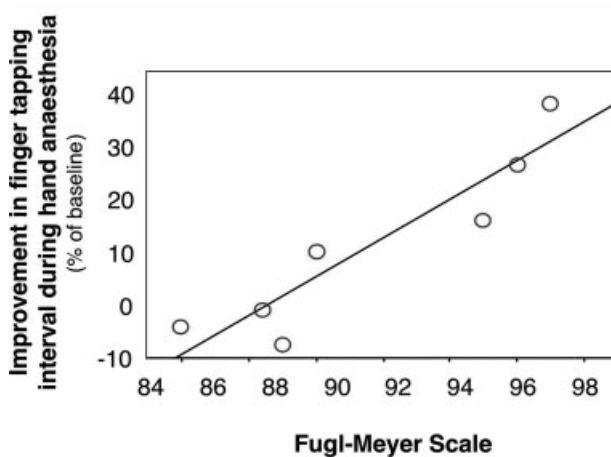

Fig 3. In patients with better motor function (upper half of Fugl-Meyer scale [FMS] in median split), the improvement in finger-tapping intervals during hand anesthesia (second measurement in Fig 2) correlated with degree of baseline muscle strength (as assessed with the FMS) (r = 9.2; p < 0.01).

mal interhemispheric interactions recently documented in patients with chronic stroke,[43] a process possibly mediated through regulation of the neurotransmitter GABA.[17]

All chronic stroke participants in this cross-sectional study initially were paralyzed (MRC below 2) but, over time, recovered to the point that they could successfully perform both motor tasks. The finding that gains in tapping speed were more prominent in patients with relatively better baseline performance (see Fig 3) suggests that a "minimum" degree of function may be required for this effect to occur.

Based on our results and those of others, the following model could be formulated: Motor performance of the paretic hand could be influenced by different operational strategies (Fig 4). (1) Reduction of somatosensory input from the intact hand, as in cutaneous anesthesia, leads to performance improvements in the other hand in healthy volunteers[9] and in patients with chronic stroke (see Fig 4A). These findings are consistent with the proposed beneficial influence of immobilization of the intact hand (which reduces somatosensory input from the immobilized limb) on training-dependent motor improvements in the weak hand of chronic stroke patients undergoing contraint-induced (CI) therapy.[5,46,47] (2) Increased somatosensory input from the paretic hand may improve motor func-

tion[48–53] (see Fig 4B), a finding consistent with the documented beneficial effect of massed motor training (which, in addition to the purely motor effects, increases somatosensory input from the paretic hand).[5,46,47] (3) Anesthesia of a body part proximal to the paretic hand (upper arm, see Fig 4C) may constitute another beneficial option to influence hand motor function.[54] In this case, anesthesia of the affected upper limb in patients with chronic stroke leads to training-dependent improvements in motor function of the paretic hand, consistent with the view that the cortical representation of the paretic hand extended over the nearby deafferented upper-arm representation.[55]

In summary, our results indicate that somatosensory input originating in the intact hand influences motor function in the paretic hand of patients with chronic stroke and could possibly modulate the beneficial effects of motor training. These findings may be relevant for the design and optimization of neurorehabilitative strategies after stroke.
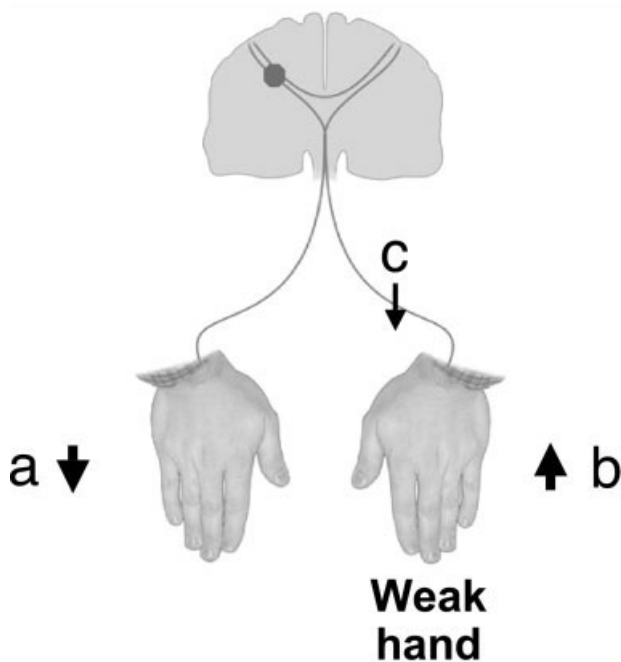
Fig 4. Motor performance of the paretic hand could be influenced by different operational strategies, including reduction of somatosensory input from the intact hand, as determined in this study (A); increased somatosensory input from the paretic hand[48–53] (B); and anesthesia of a body part proximal to the paretic hand (C).[54]

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