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Reorganization of motor output in the non-affected hemisphere after stroke

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Summary

Motor evoked responses to focal transcranial magnetic stimulation were investigated over the unaffected hemisphere in 15 patients with hemiparesis after ischaemic stroke and compared with data from normal control subjects. Whereas responses to muscles ipsilateral to the stimulated hemisphere could only be elicited at maximal intensities in two out of 12 normal control subjects, such ipsilateral responses were recorded after stimulation of the unaffected hemisphere in patients with poor recovery after stroke at significantly lower thresholds, but not in patients with good recovery. These responses occurred with a somewhat longer (on average 6 ms) latency than the typical contralateral response. The duration of the silent period ipsilateral to stimulation of the unaffected hemisphere was longer than in control subjects. Also the contralateral threshold for the unaffected hemisphere was elevated in comparison with the control group. In one patient, who developed mirror movements after stroke, the ipsilateral threshold was exceptionally low and the latency of the ipsilateral response identical to that seen contralaterally. It is concluded that the motor outputs in the unaffected hemisphere are significantly changed after stroke, including the unmasking of ipsilateral corticospinal projections. However, these pathways seem to be of little significance for recovery, as the existence of these responses was not correlated with clinical improvement. The unaffected hemisphere after stroke shows plastic changes in motor output organization after a contralateral lesion.

Keywords: transcranial magnetic stimulation; stroke; mirror movements; motor recovery

Abbreviation: MEP = motor evoked potential

Introduction

There is evidence from different sources that ipsilateral projections may be involved in restoration of function after hemispheric stroke. In their clinical investigations, Colebatch and Gandevia (1989) and Colebatch *et al*. (1990) found motor weakness on the ipsilateral side in patients with hemispheric stroke. Thilmann *et al*. (1990) described changes of muscular reflexes on the unaffected as well as the affected side. Also hemispherectomy in young patients operated on for intractable epilepsy did not lead to a complete hemiplegia, but only to a disturbance of selective and skilled finger and hand movements. Hömberg *et al*. (1991) and Benecke *et al*. (1991) demonstrated, by transcranial magnetic stimulation, the existence of an ipsilateral projection to proximal arm muscles in such patients.

In normal subjects a short inhibition of tonically activated ipsilateral muscles is found after focal transcranial magnetic stimulation (Wassermann *et al*., 1991). There have also been episodic reports of responses in stroke patients in muscles of the affected side after stimulation of the unaffected (ipsilateral) hemisphere (Britton *et al*., 1991). However, there are only few studies (Carr *et al*., 1993) of such ipsilateral projections in patients with hemispheric lesions investigated in young patients aged 2–26 years. Twenty-four out of 33 of these young patients had congenital hemispheric lesions and only five had lesions acquired between the ages of 2 and 23 years. In a short report (Turton *et al*., 1995) and in a recent published study (Turton *et al*., 1996) disinhibition of ipsilateral motor evoked potential (MEP) responses of the unaffected hemisphere to proximal limb muscles, and in a few cases also to distal hand muscles, was reported.

In this study we investigated the presence of ipsilateral projections in adult stroke patients with unilateral circumscribed lesions and in normal control subjects, using transcranial magnetic stimulation, in order to clarify whether the

ipsilateral corticospinal projections contribute to possible motor recovery. Other changes (silent periods, thresholds) after stimulation of the unaffected hemisphere were also recorded in order to look for plastic changes in motor outputs after unilateral lesions. These findings were then compared with the degree of functional recovery after stroke.

Methods

Twelve normal control subjects (mean age 50.4 ± 10.4 years, range 28–67 years; eight female and four male) and 15 patients (mean age 53.0 ± 11.0 years, range 29–70 years; four female and 11 male) in a chronic state after a hemispheric stroke (mean time since stroke, 18 ± 21 months) participated in this study. All patients initially had a severe hemiparesis with complete loss of hand function. Five of them showed a good recovery (good recovery-group), with either completely normal hand function or minor residual coordination problems but full strength, whereas the remaining patients recovered incompletely (incomplete-recovery group) with brachio-facial hemiparesis remaining and significant reduction of hand function. The degree of paresis of the hand was scored in a modified version of the Medical Research Council score for peripheral paresis encompassing simple grasp functions. The contralateral stimulation threshold for a response in the affected thenar muscle, in its relaxed state, was evaluated during the routine examination after admission, by increasing the stimulation intensity in 10% steps, starting at 40% of the maximum output of the magnetic stimulator, to find the lowest intensity at which a response of $\geqslant$50 μV could be recorded.

In the incomplete-recovery group, the mean threshold for eliciting a response on the affected side, when stimulating the contralateral hemisphere was elevated to 59.4 ± 23.2% of maximal stimulator output. In one patient (Patient 1), no contralateral response could be elicited at all, with stimulation of the affected hemisphere (the location of the stroke was derived from the acute post-stroke CT-scan). In one patient (Patient 2) no clear lesion was detectable in the acute CT-scan (1 day after the stroke). In the incomplete-recovery group only four patients showed subcortical lesions and in the good-recovery group it was four out of five patients. The patients were admitted for rehabilitation in a chronic state after their stroke. The contralateral MEP threshold at the affected side was determined during the routine clinical examination. For clinical and demographic details *see* Table 1.

One patient from the incomplete-recovery group developed mirror movements on the unaffected side after the stroke, when moving the affected hand. These movements were clearly visible with supination or fist clenching of the affected arm.

The contralateral and ipsilateral thresholds for the thenar muscle were determined in all subjects in the normal control group. All subjects gave informed consent. The stimulation protocol was approved by the ethics committee of the Heinrich-Heine-University.

Stimulation procedure

All subjects sat upright in a chair. The response was recorded with bipolar surface EMG electrodes attached to the skin over the thenar muscles of the right and left hands. Data were transmitted after pre-amplification by a telemetric device to a PC for storage and further off-line processing. After being sampled at 1 ms intervals, the EMG was rectified and averaged over groups of 10 single trials for each condition. The stimulus was applied by a Magstim 200 stimulator using a focal figure-of-eight shaped coil (diameter of each coil = 7.5 cm) with a maximal magnetic field of ~2.5 tesla (=100% stimulation intensity). The coil was held at an orientation of 45° lateral to the midline on each hemisphere with the same side always on top, resulting in a posterior-lateral to anterior-medial directed current flow.

The contralateral and ipsilateral thresholds at the unaffected hemisphere were also determined, using the above-described focal coil, applied at the position giving the highest response amplitude in the target muscle. For the baseline, the unaffected thenar contraction was held at 10% of maximal voluntary force, using a grip force-meter. In the paretic muscles, this type of control is not possible, so a surface EMG was used to monitor background muscular activity continuously, to allow analysis of responses on a 'constant' background. For determination of contralateral thresholds, a series of 40 stimuli were given in randomized order at four different intensities, increasing in 5% steps around the estimated contralateral threshold. Responses were averaged selectively for each intensity step. For determination of the ipsilateral threshold, a series of 30 stimuli were initially randomized over intensities of 70%, 80% and 90% and, if necessary, additional lower intensities were applied thereafter. The highest intensity tolerated by all subjects was 90% of the maximum stimulator output.

The EMG responses were full-wave rectified and averaged over 10 trials for each stimulation intensity.

Threshold was defined as the lowest intensity in a series, at which a clear increase (positive response) or decrease (negative response in the case of the silent period) of the rectified averaged EMG could be obtained (of $\geqslant$25% of the background activity, determined over a 100-ms pre-stimulus interval) (*see* Fig. 2). Responses were defined as absent when no response was obtainable, even at highest possible intensities. In most normal subjects, positive ipsilateral responses were absent, even at the highest tolerated stimulation intensity of 90% of maximum, so a mean threshold for ipsilateral responses could not be estimated in the normal control group. Therefore, the excitability of ipsilateral projections in normal control subjects and patients was compared using the number of positive responses at a stimulation intensity of 90% of maximum stimulator output, with the χ^2 test for contingency tables (Sachs, 1984). The duration of the silent period was defined as the interval from the stimulus to the recovery of the averaged rectified EMG to the pre-stimulus, spontaneous level of EMG activity.

Table 1 *Demographic and clinical data of the two groups of patients*

Patient	Sex	Age (years)	Lesion site identified on CT-scan	Time since stroke (months)	Upper limb function	Gait	Tone	Aphasia	Other deficits
Patients with incomplete recovery*									
01	M	29	Internal capsule and cortex of the medial cerebral artery region; left hemisphere	27	No visible movement, but surface EMG recordable in thenar muscle	Gait freely possible, but disturbed pattern	Spasticity	No	–
02	M	67	Not to localize in acute examination; left hemisphere	16	No visible movement, but surface EMG recordable in thenar muscle	Wheel chair-bound	Contractures	No	Neglect, depression, anosognosia
03	M	54	Haemorrhagic anterior internal capsule; left hemisphere	10	Selective finger movements possible	Normal	Normal	Global	–
04	M	50	Subcortical and cortical complete region of medial cerebral artery; left hemisphere	22	Flexion synergies possible only	Wheel chair-bound	Spasticity	No	Neglect, anosognosia
05	M	70	Anterior internal capsule; right hemisphere	9	Selective closure of the hand	Gait possible with assistance	Normal	Motor/ amnesic	–
06	M	66	Subcortical and cortical medial cerebral artery region; right hemisphere.	8	No visible movement, but surface EMG recordable in thenar muscle	Gait possible with assistance	Spasticity	No	Neglect
07	M	61	Subcortical and cortical left hemisphere	15	Only flexion synergies possible	Gait freely possible, but disturbed pattern	Spasticity	Motor	–
08	F	48	Subcortical left hemisphere	92	Paretic, but selective finger movements possible	Normal	Normal	Amnesic	–
09	M	60	Internal capsule and adjacent thalamus; left hemisphere	5	Paretic, but selective finger movements possible	Gait freely possible, but disturbed pattern	Normal	Motor–	
10	M	40	Subcortical and cortical posterior part of medial cerebral artery region; left hemisphere	8	Only flexion synergies possible	Gait possible with assistance	Spasticity	Motor/ amnesic	Post-stroke mirror movements
Patients with good recovery*									
11	M	51	Not to localize in acute examination;. left hemisphere	22	Normal function	Normal	Normal	Motor	–
12	F	51	Internal capsule; left hemisphere	19	No paresis, but clumsy fine movements (e.g. handwriting)	Gait freely possible, but disturbed pattern	Normal	No	Depression
13	F	52	Subcortical and cortical; left hemisphere	2	Normal function	Normal	Normal	Motor	Dysphasia
14	F	53	Subcortical haemorrhagic; left hemisphere	7	No paresis, but clumsy fine movements (e.g. handwriting)	Gait freely possible, but disturbed pattern	Normal	Motor	–
15	M	46	Subcortical and posterior part of medial cerebral artery region; right hemisphere	5	No paresis, but in some tasks fine motor control clumsy	Gait freely possible, but disturbed pattern	Spasticity in the leg	No	Depression, neglect

*Patients 1–10 showed incomplete recovery with significant motor deficits remaining. Patients 11–15 recovered with no paresis and either completely normal hand function or minor limitations in fine motor control. Patient 10 developed mirror movements after stroke.

Results

Only two of the 12 normal subjects had an excitatory ipsilateral response; this was a small excitatory response at a high stimulation intensity of 90%. The other 10 normal subjects had a purely inhibitory response on the side ipsilateral to stimulation; this was a silent period which was elicited by stimulus strengths of ~60% upwards. This silent period was of constant duration even with increasing stimulation intensities, like the typical silent period after contralateral stimulation. A typical response is shown in Fig. 1.

In all the stroke patients with incomplete recovery, a positive MEP in the affected hand was observed after stimulation of the unaffected hemisphere. Figure 2 gives an example of a typical response with a threshold of ~50% of maximum stimulation intensity. The latency of this ipsilateral response was at ~28 ms, i.e. ~5 ms longer than the latency of the usual contralateral response to the thenar muscle of the unaffected side (Fig. 2b).

In all incomplete-recovery patients an ipsilateral excitatory response could be elicited at ⩽80% (mean ipsilateral threshold = 64.0 ± 15.2%). In the good-recovery group only one patient showed an ipsilateral excitatory response (at 90% stimulator output) and in the 12 normal control subjects

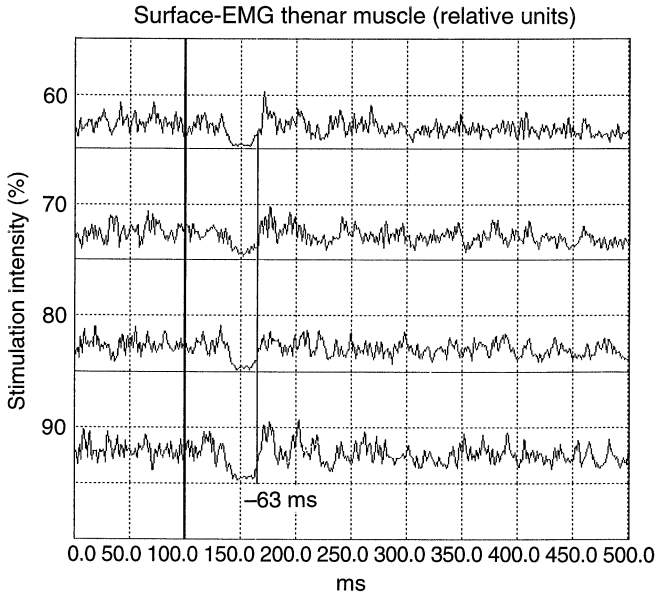

Fig. 1 Averaged (n = 10), rectified EMG showing the ipsilateral silent period without any excitatory response in a normal subject. Stimulus onset is at 100 ms. Notice the constant duration of the ipsilateral silent period even with different stimulation intensities.

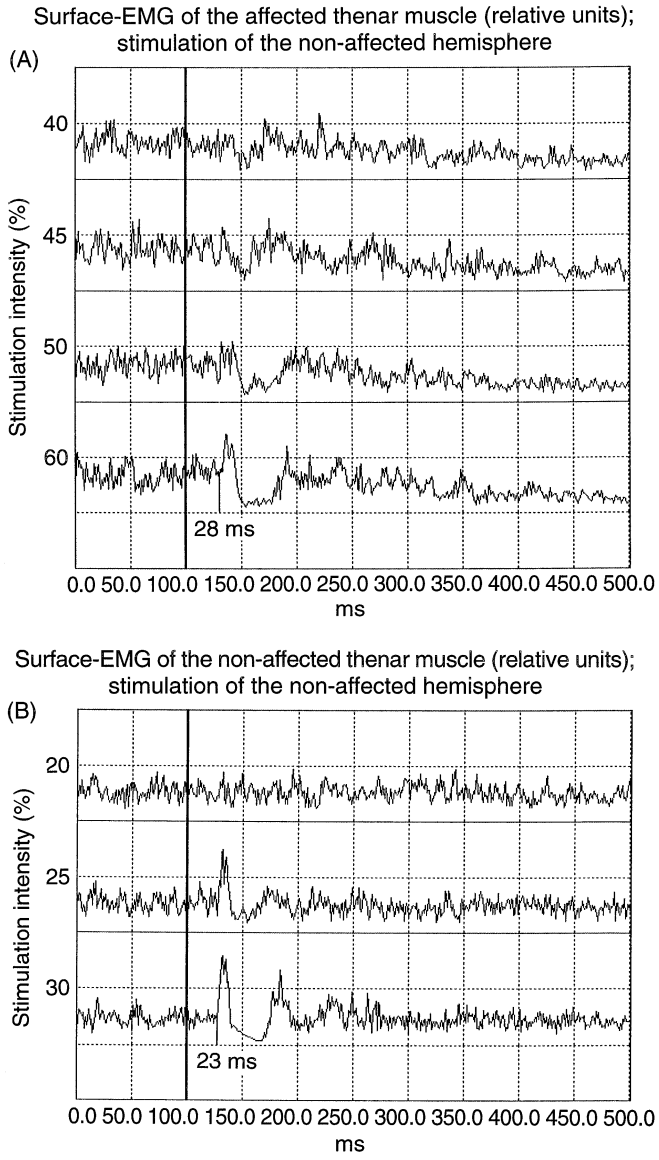

Fig. 2 Averaged responses ($n = 10$) after stimulation of the unaffected hemisphere in one patient of the incomplete-recovery group with remaining severe hemiparesis: averaged rectified surface EMG of (**A**) the ipsilateral affected and (**B**) the contralateral unaffected, tonically pre-activated thenar muscle. Notice the onset of an ipsilateral MEP at 50% intensity and the latency difference between ipsilateral and contralateral MEPs (28 and 23 ms, respectively). Stimulus onset is at 100 ms.

only two showed an ipsilateral excitatory response at 90% stimulator output. The number of subjects with positive excitatory ipsilateral responses at stimulation intensities of 90% differed significantly between the incomplete-recovery group and both the good-recovery group and the normal control group (both $P \leqslant 0.01$, two-tailed χ^2 test for four field contingency tables).

In the incomplete-recovery group the latency of the ipsilateral responses averaged 27.0 ± 3.4 ms and hence was ~6 ms longer than the latency of the corresponding contralateral response (21.3 ± 1.25 ms) or the latency

Table 2A *Motor responses in normal subjects*

Subject	MEP (contralateral)		MEP (ipsilateral)	
	Threshold (%)*	Latency (ms)	Threshold (%)*	Latency (ms)
N1	15	20	90	25
N2	15	21	>90	–
N3	20	21	>90	–
N4	30	23	>90	–
N5	15	20	90	26
N6	25	19	>90	–
N7	20	22	>90	–
N8	20	22	>90	–
N9	20	21	>90	–
N10	25	21	>90	–
N11	25	19	>90	–
N12	30	21	>90	–

*Percentage of maximum output from the magnetic stimulator.

of the contralateral responses in normal control subjects (21.0 ± 1.22 ms).

In normal subjects the duration of the ipsilateral silent period was 57.0 ± 15.2 ms, averaged over intensities of 0, 10 and 20% above the threshold of the ipsilateral inhibitory response. In patients, the ipsilateral silent period after stimulation of the unaffected hemisphere was significantly longer. In the good-recovery group the duration of the ipsilateral silent period averaged 75.6 ± 7.8 ms and in the incomplete-recovery group it was 87.6 ± 27.7 ms. The difference from the normal control subjects was significant in both cases ($P \leqslant 0.01$, two-tailed t test).

An overview of the individual ipsilateral and contralateral thresholds and latencies in all three groups of subjects is given in Table 2. The threshold for the contralateral inhibitory response was almost the same as the threshold for the contralateral excitatory response period in the normal control group, so the threshold for the contralateral silent period is not shown in Table 2.

Figure 3 summarizes the mean group data for the duration of the silent period, and ipsilateral and contralateral MEP threshold data comparing the unaffected hemisphere in the two patient groups with those in normal control subjects. In the normal control subjects, the threshold for contralateral MEP in the thenar muscles was 19.0 ± 6.5% of maximum stimulator intensity. In patients with poor recovery it was elevated to 25.9 ± 3.0%, and in patients with good recovery to 30.0 ± 5.0%. The differences between the thresholds of both patient groups and the thresholds of the normal control subjects was significant in both cases ($P \leqslant 0.05$, two-tailed t test).

All of the patients showed this identical pattern except one (Patient 10 in Table 1); this patient was the only one showing mirror movements in the unaffected hand while moving the affected hand. This patient's threshold for ipsilateral excitatory MEP responses after stimulation of the normal hemisphere was extremely low, when compared

Table 2B *Motor responses in hemiparetic patients*

Patient	Affected hemisphere	Unaffected hemisphere			
	MEP (contralateral)	MEP (contralateral)		MEP (ipsilateral)	
	Threshold at rest (%)*	Threshold (%)*	Latency (ms)	Threshold (%)*	Latency (ms)
1	NR†	25	21	60	26
2	30	30	21	80	28
3	60	30	19	80	25
4	90	25	21	60	27
5	65	25	23	45	28
6	60	25	21	80	26
7	100	25	23	60	35
8	50	30	20	70	25
9	40	25	22	70	29
10	40	20	22	35	22
11	ND‡	25	23	>90	–
12	ND‡	35	21	>90	–
13	ND‡	35	19	90	31
14	50	25	21	>90	–
12	40	30	24	>90	–

*Percentage of maximum output from the magnetic stimulator. †NR = no response at any intensity up to 100%. ‡ND = not determined because there was no paresis, even at admission. The MEP-results from the affected hemisphere were evaluated during routine electrophysiological diagnostic tests. They were measured at rest in a reclining position with the circular coil of 9.5 cm diameter of the Cadwell stimulator. There were no excitatory responses at stimulation intensities of ⩽90% of maximum output.

with that of the other nine patients of the incomplete-recovery group (35% versus 67.2 ± 12.0%). Furthermore, the latency of the ipsilateral response was identical to that of the contralateral response (22.0 ms) (Fig. 4A and B). Hence it was much shorter than that of the other nine patients (27.6 ± 3.1 ms) and was well within the range for normal contralateral responses (21.0 ± 1.22 ms).

Discussion

Ipsilateral inhibitory responses are easily obtainable in normal subjects and patients (Wasserman *et al*., 1991) at relatively low stimulation intensities. Ipsilateral excitatory responses in the distal hand muscles, however, are only rarely found in normal subjects (Farmer *et al*., 1990; Wasserman *et al*., 1991; Carr *et al*., 1994). Wasserman *et al*. (1994) reported, in a mapping paradigm, that in each of six normal subjects at least one stimulating position yielded a positive ipsilateral response in a statistical amplitude test. In nearly all cases these positions were different from the optimal position for eliciting contralateral responses. Our data also show that ipsilateral excitatory responses can only rarely be recorded from positions optimal for contralateral responses in normal control subjects, but regularly in patients with residual hemiparesis after stroke, when stimulating the unaffected hemisphere.

As we used a coil with a fairly high magnetic output and large diameter, it might be argued that these ipsilateral responses were due to stimulation of the opposite intact hemisphere by spurious magnetic fields or far reaching eddy currents. In the normal control subjects this possibility cannot be excluded completely. However, even in normal control subjects, the relative independence of ipsilateral silent period duration from stimulation intensity, in contrast to the contralateral responses (Uozumi *et al*., 1992; Roick *et al*., 1993), does not support this possibility. In the patients, other findings further exclude this possibility: (i) the latency of the ipsilateral excitatory response is, on average, 6 ms longer than the latency of the contralateral response; (ii) in all patients the opposite hemisphere was severely lesioned with either completely missing MEPs or extremely elevated thresholds; and (iii) in the normal control subjects, the contralateral MEPs had a threshold which was three times lower than in patients. In contrast, the threshold for ipsilateral responses was higher in normal control subjects than in the intact hemisphere of patients.

Possible anatomical connections underlying these ipsilateral responses include ipsilateral projections of the pyramidal tract, which are known to account for a variable but small proportion of the whole fibre mass (Brodal, 1969; Wiesendanger, 1981). However, it is known that at least a considerable proportion of these fibres do cross to the contralateral side at the segmental level (Liu and Chambers, 1964). On the other hand, a considerable amount of corticospinal ipsilateral degeneration was found after cortical lesions by Liu and Chambers (1964), and by Kuypers and Brinkmann (1970). Hence the anatomical and neurophysiological data are inconclusive as to what degree ipsilateral pyramidal fibres are responsible for the detectable ipsilateral responses in patients. Also a corticoreticular–spinal route is possible (Brodal, 1969). The latter could possibly explain the longer latency of the ipsilateral responses due to smaller fibre diameters and multiple intercalated synapses.

The functional impact of the obtainable ipsilateral

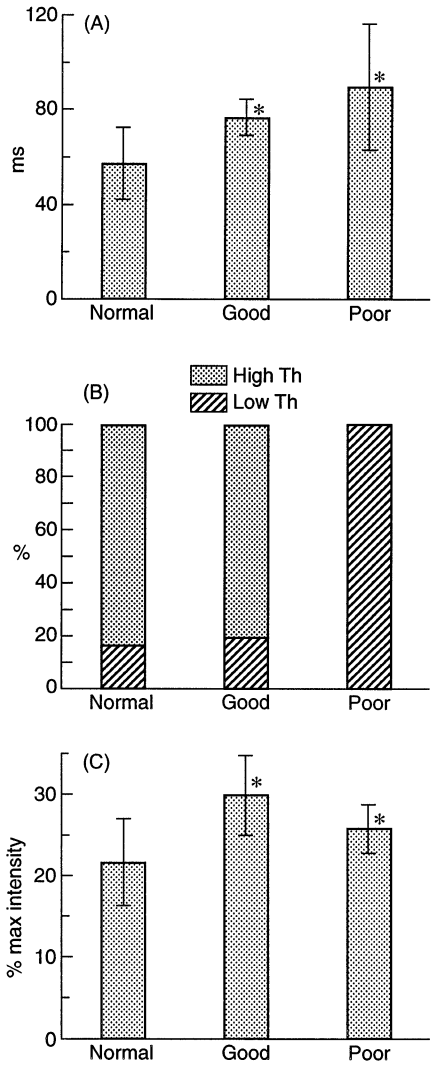

Fig. 3 Summary of results of stimulation of the unaffected hemisphere averaged for all patients as compared with normal control subjects. (**A**) Mean duration of ipsilateral silent period for the unaffected thenar in the incomplete-recovery and good-recovery patient-groups (*see* 'poor' and 'good', respectively), showing anlonger duration than normal control subjects (*$P \leqslant 0.05$, two tailed t test). (**B**) Percentage of subjects showing an ipsilateral excitatory response at 90% stimulation intensity. Both normal control subjects and patients of the good recovery group showed significantly less responses than the incomplete-recovery group ($P \leqslant 0.01$, two-tailed χ^2 test for four-field-contingency). In the key, 'high Th' (and 'low Th') indicate that the ipsilateral threshold is >90% (and ⩽90%) of the maximum output of the stimulator. (**C**) Contralateral MEP-threshold for the unaffected thenar in the incomplete-recovery (poor), the good-recovery (good) groups of patients and normal control subjects, showing an increased threshold for the unaffected hemisphere in both patient groups (*different from normal control subjects: $P \leqslant 0.05$, two-tailed t test).

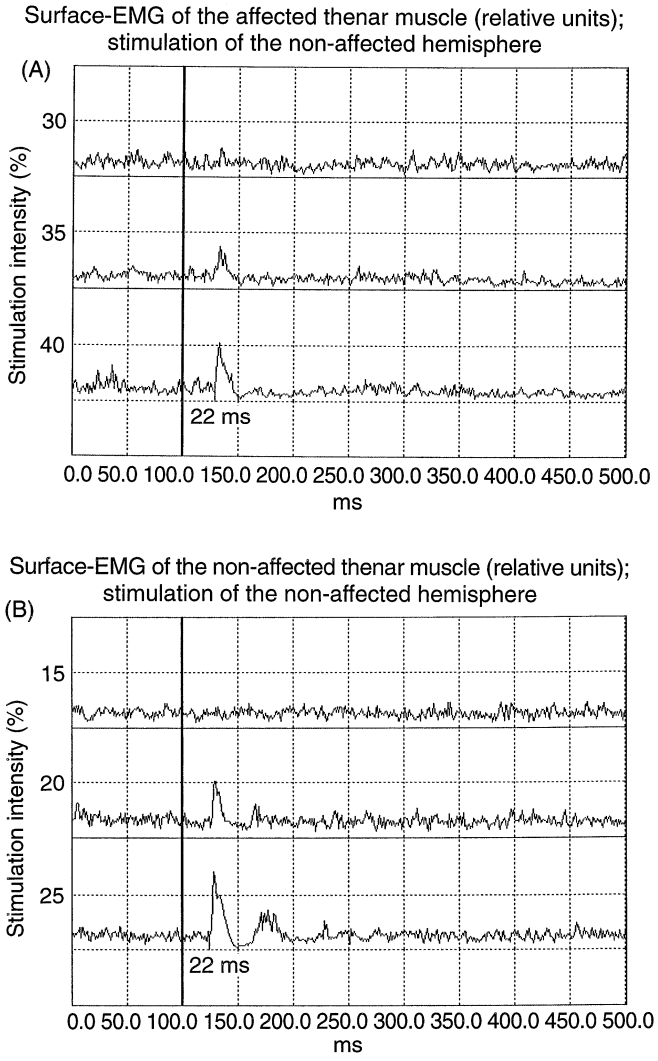

Fig. 4 Averaged responses after stimulation of the unaffected hemisphere in the one patient of the incomplete-recovery group with mirror movements averaged ($n = 10$) rectified surface EMG of (**A**) the ipsilateral affected and (**B**) the contralateral unaffected, tonically pre-activated thenar muscle. Note the identical latency of the ipsilateral and contralateral MEPs (22 ms each). Stimulus onset is at 100 ms.

responses is unclear. In our study these projections were obtained in all patients with only partial recovery and remaining paresis after stroke including severely paretic extremities with nearly completely missing hand functions. In contrast, the patients with good recovery did not differ from normal control subjects. It must therefore be concluded that the underlying projections had little functional significance for recovery and were not used for motor control. The ipsilateral responses therefore appear to be the consequence of a disinhibition, or unmasking, of a normally suppressed or inhibited pathway, rather than a sign of a restorative change to compensate for the deficit. [Recently in a TMS study, Turton *et al*. (1996) showed largely the same results for the ipsilateral responses in distal muscles on the affected side in stroke patients, with no responses in 11 trials in patients with good recovery and five in 49 trials in patients with poor recovery. The lower number of total responses may be explained by their use of a different coil and a lower stimulation intensity.] However, the contribution of this unmasking of an existing pathway to motor recovery appears

to be limited in the majotity of patients. The situation appears to be somewhat different in those patients who develop mirror or associated motor activity after cerebrovascular lesions.

In one of our patients, the one who developed 'mirror movements' after the stroke, the lower threshold and shorter latency of the ipsilateral responses after stimulation of the normal hemisphere were possibly due to ipsilateral collaterals of pyramidal fibres. In a study with young patients with perinatally acquired hemiparesis (Carr *et al*., 1993), the possibility of such collaterals was suggested by correlation analysis of single motor unit responses. Similar ipsilateral responses have been observed in subjects with congenital mirror movements (Konagaya *et al*., 1990) and Kallmann's syndrome (Danek *et al*., 1992). Our post-stroke patient with acquired mirror movements also belonged to the partly recovered group but, nevertheless, had achieved some considerable progress in motor function from an initially complete plegia of the affected arm. Thus it appears that, in this patient, a different mechanism for recovery was present. This patient had a subcortical stroke, possibly sparing transcallosal connections between the motor cortices.

From the literature it is known that only a small percentage of patients develop mirror movements or associated movements during recovery after stroke (Fries *et al*., 1991; Weiller *et al*., 1992; Carr *et al*., 1993). The percentages, where presented, vary depending upon the definition of 'mirror movements'. Carr *et al*. (1993) showed in their study, that particularly those patients with prenatally aquired lesions developed mirror movements and they had a good functional recovery. It is unlikely that axon collaterals to the contralateral spinal cord develop after stroke, but it may be that some axon collaterals to the ipsilateral side may have been present prior to stroke, but were more inhibited than in subjects with congenital mirror movements. In a recent study, Reitz *et al*. (1996) show that, during ontogeny, ipsilateral corticospinal projections as determined by TMS are normally detectable in normal children until the age of ~10 years. These responses are more frequently detectable in proximal than in distal upper extremity muscles and occur at latency differences which are somewhat longer (12 ms on average) than those in adult stroke patients. It is known that associated movements are constantly present in younger children and gradually disappear up until the age of about 10 years (Lazarus and Todar, 1987). At this time, at least on 'macroscopic' clinical examination, mirror movements disappear. On the other hand, in EMG recordings, mirrored motor-activity may still be detectable in distal upper extremity muscles in normal adults (e.g. Kristeva *et al*., 1990). It therefore appears possible that ipsilateral corticospinal efferents are normally present but become more and more inhibited during the first decade of development. After a stroke, due to lack of inhibition from the affected hemisphere, especially when the cortical fibres are involved, these connections may then become unmasked. The reason why only a few patients develop mirror movements during stroke recovery is unknown. It may be that the bilateral spinal projections mentioned above are developed to different degrees in different individuals, becoming clinically evident only in extreme cases. Alternatively, different topography of the lesion may lead to different degrees of unmasking. Fries *et al*. (1991), Libman *et al*. (1992) and Weiller *et al*. (1992) found a high percentage of mirror or associated movements together with good recovery in patients with isolated capsular lesions. In these cases the remaining inhibitory transcallosal influence on the unaffected hemisphere may be modulated in a more functionally useful way to bring ipsilateral projections from the unaffected hemisphere into operation, compared with cases with lesions closer to the motor cortex, where these connections are interrupted. Also the one patient with mirror movements in our study showed an initial, but incomplete, recovery.

Our data in adults demonstrate further changes in the function of the unaffected hemisphere after stroke; the duration of the ipsilateral silent period is significantly longer in both patient groups than in normal control subjects. This change may be interpreted either as a modulatory influence of the affected hemisphere on efferences of the unaffected side or as a modulation of the unaffected hemisphere itself, depending on the route of the ipsilateral inhibitory response.

Also the average stimulus threshold for contralateral MEP when stimulating the unaffected hemisphere was significantly higher in the patients than in normal control subjects. This difference was not as impressive as for the ipsilateral responses and, in addition, it did not correlate with the severity of remaining deficits in that it showed the highest difference for the good-recovery group. Bilateral affections could not be excluded completely, but EEG and imaging data in our patients showed no evidence of the involvement of both hemispheres. In previous studies on stroke patients, there have been no descriptions of similar changes of the contralateral MEP-threshold in the unaffected hemisphere (Hömberg *et al*., 1991). This may be due to the fact that in the previous study non-focal coils were used and the subjects were in a relaxed state.

In conclusion, the present results provide more evidence that in hemiparetic patients adaptive changes do occur in the unaffected hemisphere. The functional impact of pre-existing ipsilateral corticospinal connections varies depending on the precise pattern of unmasking, or on more balanced disinhibition of these pathways.

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