

# The silent period induced by transcranial magnetic stimulation in muscles supplied by cranial nerves: normal data and changes in patients

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## Abstract

**The silent period induced by transcranial magnetic stimulation of the sensorimotor cortex (Magstim 200, figure of eight coil, loop diameter 7 cm) in active muscles supplied by cranial nerves (mentalis, sternocleidomastoid, and genioglossus) was studied in 14 control subjects and nine patients with localised lesions of the sensorimotor cortex. In the patients, measurements of the silent period were also made in the first dorsal interosseus and tibialis anterior muscles. In the controls, there was a silent period in contralateral as well as ipsilateral cranial muscles and the duration of the silent period increased with increasing stimulus intensities. The mean duration of the silent period was around 140 ms in contralateral mentalis muscle and around 90 ms in contralateral sternocleidomastoid muscle at  $1.2 \times$  threshold stimulation strengths. Whereas the duration of the silent period in ipsilateral mentalis muscle was shorter than on the contralateral side it was similar on both sides in sternocleidomastoid muscle. In patients with focal lesions of the face associated primary motor cortex and corresponding central facial paresis, the silent period in mentalis muscle was shortened whereas it was unchanged or prolonged in limb muscles (first dorsal interosseus, tibialis anterior) with stimulation over the affected hemisphere. By contrast, in a patient with a lesion within the parietal cortex, the silent period in mentalis muscle was prolonged with stimulation of the affected side.**

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**Keywords:** transcranial magnetic stimulation, cranial nerves, sensorimotor cortex, silent period

Transcranial magnetic stimulation has been widely used to study the function of the corticospinal pathways in humans.<sup>1</sup> The responses it evokes are thought to be generated by excitation of corticomotoneuronal pathways at the cortical or just subcortical level in the motor cortex and to be mediated by fast conducting corticospinal pathways.<sup>1,2</sup>

After the early compound muscle action potential (CMAP) evoked by transcranial

magnetic stimulation in limb muscles a period of electromyographic (EMG) silence (silent period) lasting some 200 ms in small hand muscles can be found if the target muscle is tonically active.<sup>3-8</sup> The duration of the silent period follows a proximodistal gradient in the upper limb muscles, being longer in small hand muscles than in proximal arm muscles. As to precisely what structures are involved in the generation of the silent period there is an increasing amount of data suggesting that it is not due to changes in  $\alpha$  motoneuron activity but to changes in pyramidal cell excitability.<sup>3,6,8-11</sup>

Apart from the study of distal limb muscles, several reports exist on activation of corticonuclear fibres supplying cranial nerve motoneurons using transcranial magnetic stimulation.<sup>12,13</sup> With bilateral recordings two types of responses can be seen in muscles supplied by cranial nerves: purely ipsilateral short latency responses and bilateral responses of longer latency. On the basis of latency, amplitude, configuration, and reaction to facilitatory manoeuvres, these two types were considered to originate from unilateral direct excitation of cranial nerves at proximal sites and the corticonuclear system respectively.<sup>12,13</sup> The bilateral (corticonuclear) long latency responses reflect the bilateral cortical input to the brainstem nuclei of cranial nerves.

The first aim of the present study was to describe the characteristics of the silent period induced by transcranial magnetic stimulation in facial, neck, and tongue muscles in normal subjects. If it is assumed that the silent period in these muscles is also generated cortically, a silent period should also exist in cranial muscles ipsilateral to the site of stimulation, given the bilateral corticonuclear projection.

Secondly, we wanted to examine changes in the duration of the silent period in muscles supplied by cranial nerves in patients with unilateral cortical lesions. Alterations of the silent period in distal limb muscles of patients with cortical and subcortical or thalamic lesions have been described.<sup>4,5,14</sup> In patients with lesions of the primary motor cortex itself the silent period was shortened<sup>14</sup> or abolished<sup>10</sup> in muscles contralateral to the hemispheric lesions. In patients with lesions in other motor competent cortical areas which are afferent to the primary motor cortex a prolongation of the silent period occurred.<sup>14</sup>

Some of the data from the present investigation have appeared in abstract form.<sup>15</sup>

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## Methods

Experiments were performed in 14 control subjects and nine patients. All gave their informed consent for the study and the project was approved by the local ethics committee.

### CONTROLS

Fourteen control subjects (11 men, three women, mean age 34.2 (range 19–52) years) were chosen from among the authors and other members of the department. Subjects with a history of hypertension, headache, a cerebrovascular event, or subjects over the age of 60 were excluded. This last criterion was used to reduce the possibility of subclinical cerebrovascular abnormalities.

### PATIENTS

Table 1 lists the clinical details of the patients. Patients (five men, four women, mean age 59.1 (range 41–75) years) were selected among consecutive patients seen as inpatients in our department, who had a unilateral hemispheric lesion due to vascular accident or tumour. Patients unable to cooperate or confined to bed were excluded. Clinical data and results of investigations were obtained from the patients' records. Two patients (3 and 5) reported previous cerebrovascular events. Patient 3 had had a left hemispheric infarct with global dysphasia and right facial weakness one year before the study and patient 5 had had a left hemispheric infarct with right sided hemiparesis, including the face, with complete remission after a few weeks, four years previously. The localisation of the lesions in the patients

was established by MRI and CT performed during the stay in hospital.

### STIMULATION PROCEDURE AND RECORDINGS IN MUSCLES SUPPLIED BY CRANIAL NERVES IN CONTROLS AND PATIENTS

Subjects and patients were seated in a comfortable chair. Transcranial magnetic stimulation was performed with a conventional Nova-metrix 200 stimulator (Fa Madaus, Magstim Company UK) with a maximum output of 2.0 Tesla, connected to a figure of eight magnetic coil, each loop having a diameter of 7 cm. Technical information about the stimulator can be found elsewhere.<sup>11 16</sup>

The coil was held over the skull with the maximum current in the coil flowing in an anteroposterior direction. The centre of the coil was placed consecutively over both hemispheres about 9 cm lateral and 3 cm anterior to a line connecting the vertex and the external auditory meatus. The precise coil position was then adjusted to give a response of maximum size in the contralateral cranial muscle at a given stimulus intensity. The optimal position of the coil was marked on the skull for better retrieval. Before each recording session the threshold for evoking cortical muscle responses was determined for each muscle with the subject or patient at rest and the coil held over the optimal spot. Threshold was defined as the lowest stimulus intensity (as a percentage of the maximal output of the device) with which a defined cortically evoked response of at least 100  $\mu$ V peak to peak amplitude could be obtained on three consecu-

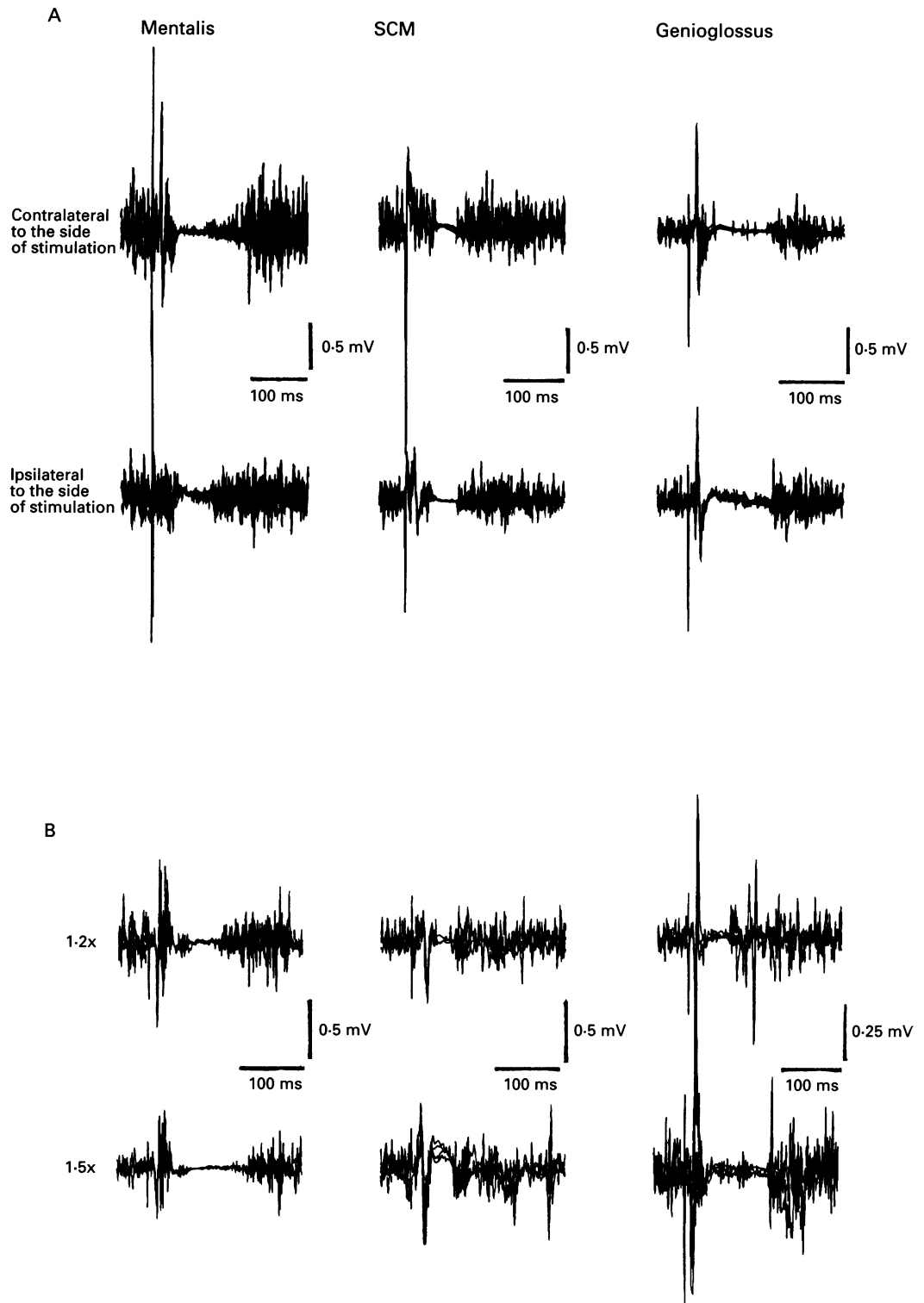
Table 1 Clinical data for patients

Patient	Age (y)	Sex	Localisation	Type	Interval	Clinical findings	CMCT/Amplitude	
							Hand	Leg
1	49	F	Right parietal	TU*	33 months	CN normal, mild sensory deficits left arm, no dysphasia	Normal	Normal
2	61	M	PMC	Infarct	4 months	Initially mild lower facial weakness, monoparesis left lower arm, no dysphasia	↑ CMCT left	Normal
3	75	F	Left fronto-parietal	Infarct	5 days	CN normal, in 1992 dysphasia and right facial weakness, sensorimotor dysphasia, paresis right arm	↓ Amp right	Normal
4	65	F	Right fronto-parietal	Infarct	4 years	Minor hemiparesis left arm > leg, predominant left facial weakness, no dysphasia, left hemineglect and sensory deficits	Normal	Normal
5	64	M	Left postcentral gyrus	Infarct	1 year	CN normal, no dysphasia, spastic monoparesis right arm, transient right hemiparesis (including face) in 1989	↓ Amp right	Normal
6	54	M	Left PMC and striatocapsular	Infarct	2.8 months	Right facial weakness and minor motor aphasia, spastic hemiparesis right	No response right	↓ Amp ↑ CMCT
7	73	F	Left fronto-parietal	Infarct	17 days	Discrete right hemiparesis (arm > leg) sensory dysphasia, mild facial weakness	↓ Amp right	Normal
8	41	M	Right fronto-parietal	Infarct	17 days	Left hemiparesis (face > arm > leg) global dysphasia	↑ CMCT left	↑ CMCT Left
9	55	M	PMC	Infarct	3 days	Right hemiparesis (arm + face) resolving after 4 days, motor dysphasia	Normal	Normal

Amplitude and CMCT = Amplitude and central motor conduction time for the first dorsal interosseus muscle (in patient 2 the finger extensors were abnormal while variables in the first dorsal in interosseus muscle were normal) and tibialis anterior muscle; ↑ = prolongation; ↓ = reduction, CN = cranial nerves; Interval = the time between the occurrence of the lesion and the time of study; PMC = primary motor cortex.

\*Haemangioma as proved by histology, operated on in June 1990.

**Figure 1** Raw data from two normal subjects showing examples of the silent period in muscles supplied by cranial nerves. In each trace five sweeps are superimposed. (A) Recordings are shown in the muscles contralateral and ipsilateral to the side of stimulation. Note that in mentalis and genioglossus muscles during the silent period, EMG background activity is not decreased to zero. (B) the relation between the stimulus intensity (expressed relative to the threshold ( $T$ ) for contralateral responses at rest), and the duration of the silent period in contralateral muscles is shown. The silent period was longer with higher stimulus intensities only in mentalis and genioglossus muscle; it was unchanged in sternocleidomastoid (SCM).



tive trials in the contralateral target muscle. Usually a stimulation strength of  $1.5 \times$  threshold was used during the recordings. In some experiments (subjects with a high cortical threshold at rest or in whom the effect of changing the stimulus intensity was under investigation) recordings were also made using  $1.2 \times$  threshold or  $2.0 \times$  threshold stimulus intensities. In the controls the threshold of stimulation between the two hemispheres differed by 5% of the maximum output of the device in one subject for mentalis muscle, in two subjects for sternocleidomastoid muscle, and in one subject for genioglossus muscle. In

patients, except 7 and 8, there was no inter-hemispheric difference in the threshold of stimulation in the muscles under study. In patient 7 the threshold for cortical responses was 5% higher with stimulation over the affected hemisphere in both mentalis and sternocleidomastoid muscle. By contrast, in patient 8 the threshold stimulating over the affected hemisphere was 10% below the threshold of the unaffected hemisphere.

In most cases recordings were made with concentric needle electrodes (Medelec, disposable type DFC 25) inserted into the target muscles. In some subjects who did not tolerate

needle recordings surface electrodes (Dantec 13L20) with the active electrode over the muscle belly and the reference electrode 2–3 cm apart were used. In controls mentalis muscle was recorded from bilaterally in 11 subjects and sternocleidomastoid muscle in nine subjects. Recordings from the tongue musculature were made in two subjects.

Responses from mentalis muscle were recorded with needle electrodes in seven patients and with surface electrodes in two (patients 7 and 9 in tables 2 and 3). Recordings were made bilaterally except in patient 9. In addition, in patients 6, 7, and 9 bilateral recordings were also made from sternocleidomastoid muscle.

After definition of the optimal site of stimulation and threshold for a given muscle, bilateral recordings were made in tonically active muscles. The level of preactivation (20% of maximum) was monitored by audiovisual control by the subjects or patients. In both subjects and patients at least 20 stimuli were applied to each hemisphere for every muscle under study. The EMG signals were amplified using a Toennies Myograph IIR with band-pass filtering set between 20 and 3000 Hz. The data were digitalised by a CED 1401+ (Cambridge Electronic Design, UK) interface, sampled (CED, Signal Averager), and stored with a sampling rate of 5000 Hz using a personal computer for later off line analysis.

For analysis and measurements of the silent period duration the mean (SD) of 20 sweeps of 600 ms total duration was measured off line. The stimulus in each sweep was given 100 ms after the start of the sweep to record the level of EMG background activity. Trials with insufficient background activity were rejected from analysis. Because the silent period in cranial muscles most often did not terminate abruptly the duration of the silent period in these muscles was defined as the time between the onset of the magnetic stimulus and the time when EMG background activity reached at least 50% of the prestimulus level. In most cases the offset of the silent period could be determined by visual inspection (fig 1). In cases in which it was difficult to

clearly define the offset, EMG activity of the single traces was rectified and measurements of the amplitude were made before and after the stimulus. These measurements were used to determine the onset of EMG background activity after the silent period. For statistical analysis unpaired Student's *t* tests were used.

#### STIMULATION PROCEDURE AND RECORDINGS IN LIMB MUSCLES IN PATIENTS

In the patients recordings were also made from the first dorsal interosseus and tibialis anterior muscles. Surface electrodes (Dantec 13L20) with the active electrode placed over the muscle belly and the reference electrode placed either over the index finger or the medial aspect of the tibial bone were used. Stimulation was performed with a Novamatrix Magstim 200 conventional stimulator connected to a round coil (12 cm outer diameter) for stimulation of the first dorsal interosseus and a large angled figure of eight coil (outer loop diameter 13 cm) for stimulation of leg muscles. The coils were held with the centre of each coil over Cz. Threshold at rest was determined as the stimulation strength which induced a CMAP in the contralateral muscle in at least half of five consecutive trials when the muscle under study was at rest. During recordings a stimulus intensity of  $1.5 \times$  threshold was used with the muscle tonically active and under audiovisual control of the level of preactivation. Sampling and analysis procedures were otherwise identical to those used for muscles innervated by cranial nerves. Normal data regarding the silent period duration in limb muscles have been reported in a previous study.<sup>8</sup>

## Results

### CONTROLS

In the controls, transcranial magnetic stimulation of one hemisphere evoked a silent period in ipsilateral and contralateral cranial muscles. Table 2 shows the mean durations of the silent period in mentalis, sternocleidomastoid, and genioglossus muscles at various stimulus intensities. Figure 1A shows a representative example of the silent period in these muscles.

The silent period in contralateral mentalis muscle in most cases consisted of an initial period lasting around 100 ms during which the EMG background activity was suppressed and a second phase in which some tonic activity returned but was still clearly below the prestimulus level (fig 1A).

As illustrated in fig 1A and shown in table 2 the mean duration of the silent period in ipsilateral mentalis muscle was somewhat shorter than in contralateral muscles (stimulation of right hemisphere: duration = 34.3 ms,  $P = 0.013$ ; stimulation of left hemisphere: duration = 30.8 ms,  $P = 0.077$ , *t* test). This was not true for sternocleidomastoid or genioglossus muscles, in which the duration on average was the same in ipsilateral and contralateral muscles (see also fig 1A).

At  $1.2 \times$  threshold the duration of the silent period was significantly longer

Table 2 Duration and interhemispheric difference in ms (mean (SD)) of the silent period in normal subjects

Muscle	No of subjects	T (stim int)	Contralateral	Ipsilateral
<i>Stimulation of right hemisphere</i>				
Mentalis	9	1.2 × (68)	140.0 (30.2)	128.2 (26.4)
	9	1.5 × (85)	184.8 (17.2)	150.5 (32.4)
Sternocleidomastoid	9	1.2 × (93)	92.5 (18.7)	96.9 (14.2)
Genioglossus	2	1.2 × (45)	61.9 (4.0)	59.4 (5.0)
	2	1.5 × (57)	122.4 (10.0)	117.7 (14.0)
<i>Stimulation of left hemisphere</i>				
Mentalis	9	1.2 × (67)	133.7 (31.6)	118.9 (34.8)
	9	1.5 × (85)	182.2 (20.0)	151.4 (44.6)
Sternocleidomastoid	8	1.2 × (93)	87.0 (23.1)	97.9 (18.5)
Genioglossus	2	1.2 × (42)	68.7 (2.8)	57.7 (11.6)
	2	1.5 × (53)	140.2 (8.5)	135.3 (1.1)
<i>Interhemispheric difference</i>				
Mentalis	9	1.2 ×	12.9 (10.4)	20.8 (12.2)
	9	1.5 ×	17.2 (7.7)	19.4 (14.1)
Sternocleidomastoid	8	1.2 ×	9.8 (8.7)	5.4 (3.5)
Genioglossus	2	1.2 ×	6.9 (1.6)	6.6 (1.0)
	2	1.5 ×	18.5 (25.1)	17.6 (15.1)

T = Stimulus intensity in  $\times$  threshold at rest; stim int = average stimulus intensities (in parentheses) as percentage of the maximum output of the stimulating device.

Table 3 Duration in ms (mean (SD)) of the silent period in patients with unilateral cerebral lesions

Patient	Mentalis		SCM		FDI		TA	
	Affected (ipsilat)	Unaffected (ipsilat)	Affected	Unaffected	Affected	Unaffected	Affected	Unaffected
1	179 (18)*** <b>102 (32)</b>	104 (28) <b>89 (27)</b>	—	—	222 (23)***	183 (13)	258 (16)***	193 (50)
2	109 (11)*** <b>73 (19)</b>	211 ± 14 <b>Not measurable</b>	—	—	212 (14)***	170 (6)	—	—
3	95 (3)*** <b>108 (25)</b>	171 (12) <b>162 (29)</b>	—	—	241 (33)***	200 (15)	174 (38)***	126 (11)
4	63 (15)*** <b>Not measurable</b>	153 ± 9 <b>149 ± 8</b>	—	—	602 (82)***	229 (19)	348 (29)***	284 (32)
5	124 (10)*** <b>102 (22)</b>	176 ± 6† <b>163 ± 13</b>	—	—	194 (27)	169 (7)	230 (34)***	163 (10)
6	96 ± 8*** <b>100 (6)</b>	203 (7) <b>201 (7)</b>	106 (10)	104 (7)	No response	177 (7)	No response	108 (16)
7	117 (17)*** <b>113 (13)</b>	197 (7) <b>184 (19)</b>	53 (3)	55 (3)†	159 (15)***	193 (6)	244 (6)	250 (8)
8	153 (9)*** <b>144 (25)</b>	332 (14) <b>332 (15)</b>	—	—	355 (17)***	270 (37)	389 (40)	387 (45)
9	58 (5)***	163 (15)	97 (11)	96 (7)	204 (12)**	186 (10)	135 (17)	125 (17)

\*\*  $p < 0.01$ ; \*\*\*  $p \leq 0.001$  ( $t$  test for interhemispheric difference).

†  $1.2 \times$  threshold stimulus intensity.

Silent period duration in muscles ipsilateral to the side of stimulation are given in bold.

SCM = sternocleidomastoid; FDI = first dorsal interosseus; TA = tibialis anterior; — = not done.

( $P < 0.01$ ) in mentalis muscle compared with sternocleidomastoid and genioglossus muscle both for ipsilateral and contralateral responses (table 2).

The duration of the silent period in genioglossus and mentalis muscle ipsilateral and contralateral to the side of stimulation depended on the stimulus intensity (fig 1B, table 2), being longer at higher stimulus inten-

sities ( $1.2 v 1.5$  threshold;  $P < 0.05$ ). At  $1.5$  threshold differences in duration between mentalis and genioglossus muscle were not significant. Sternocleidomastoid muscle could not generally be tested at  $1.5$  threshold due to high absolute threshold and limitations of the stimulus device. However, in one subject activity in sternocleidomastoid muscle showed only a slight increase in duration of the silent

Figure 2 Raw data from mentalis, sternocleidomastoid (SCM), and first dorsal interosseus (FDI) muscles contralateral to the side of stimulation in two patients. In each graph five sweeps are superimposed. In patient 6(A) the silent period in mentalis muscle (left two panels) is significantly shorter and less well formed and the amplitude of the early direct response is reduced with stimulation of the affected compared with the unaffected hemisphere. By contrast, there is no difference in the silent period duration in sternocleidomastoid (right two panels). Comparing the duration of the silent period in mentalis muscle, patient 1(B) shows that it is significantly longer after stimulation of the affected compared with the unaffected side. By contrast, the duration of the silent period in the first dorsal interosseus muscle (right two panels in (B)) is prolonged with stimulation of the affected compared with the unaffected side.

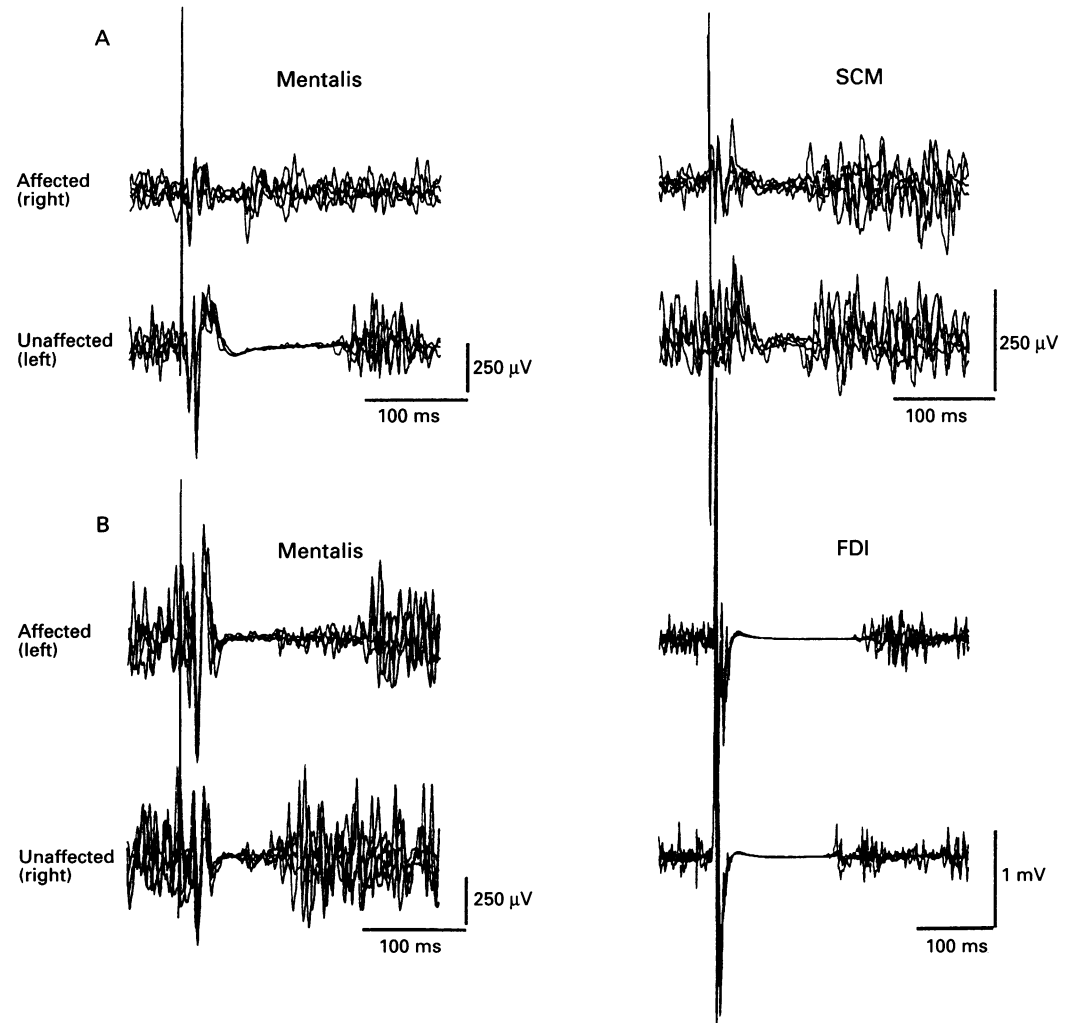
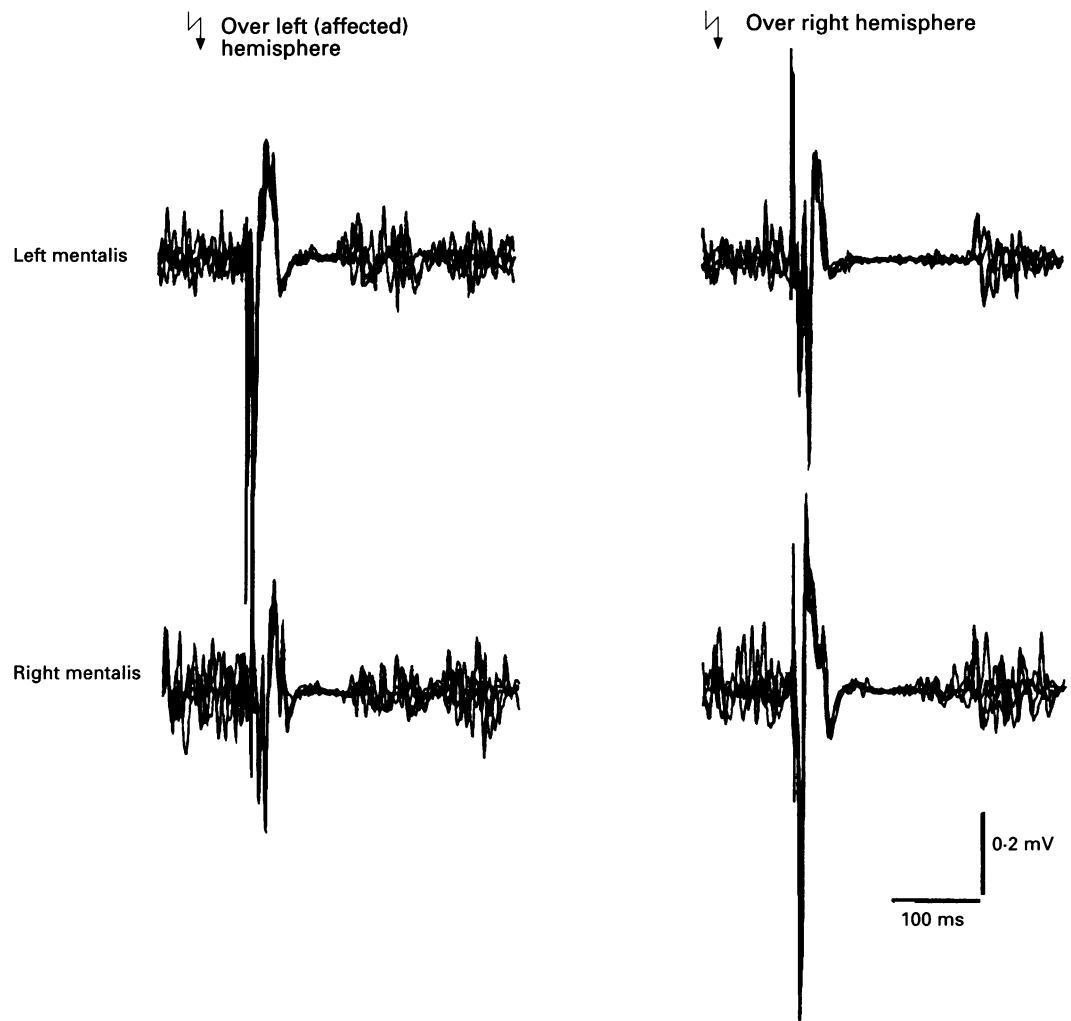


Figure 3 Raw data from mentalis muscle from patient 7. Stimulation over the affected (left) hemisphere produced a shorter silent period both in the contralateral and ipsilateral mentalis muscles compared with the silent period after stimulation of the unaffected hemisphere. Note that the direct responses in muscles ipsilateral to the side of stimulation are partly masked by the stimulus artifact, which was bigger on the side ipsilateral to the magnetic coil.



period at  $1.5 \times$  threshold stimulus intensity (Fig 1B).

The duration of the silent period was variable between subjects (see SDs in table 2). This was particularly true at low stimulus intensities ( $1.2 \times$  threshold). Comparing the duration of the silent period between the two hemispheres, there was no statistically significant difference when all subjects were taken together. The mean interhemispheric difference in the duration of the silent period in the muscles contralateral to the side of stimulation in all subjects was  $12.9$  ( $10.4$ ) ms (mean(SD)) at  $1.2 \times$  threshold and  $17.7$  ( $7.7$ ) ms at  $1.5 \times$  threshold for mentalis muscle and  $9.8$  ( $8.1$ ) ms for sternocleidomastoid muscle (table 2).

#### PATIENTS

Table 3 summarises the results for the patients and figs 2 and 3 give examples of the raw data. According to this definition, there was a significant difference in the duration of the silent period in mentalis muscle in all patients.

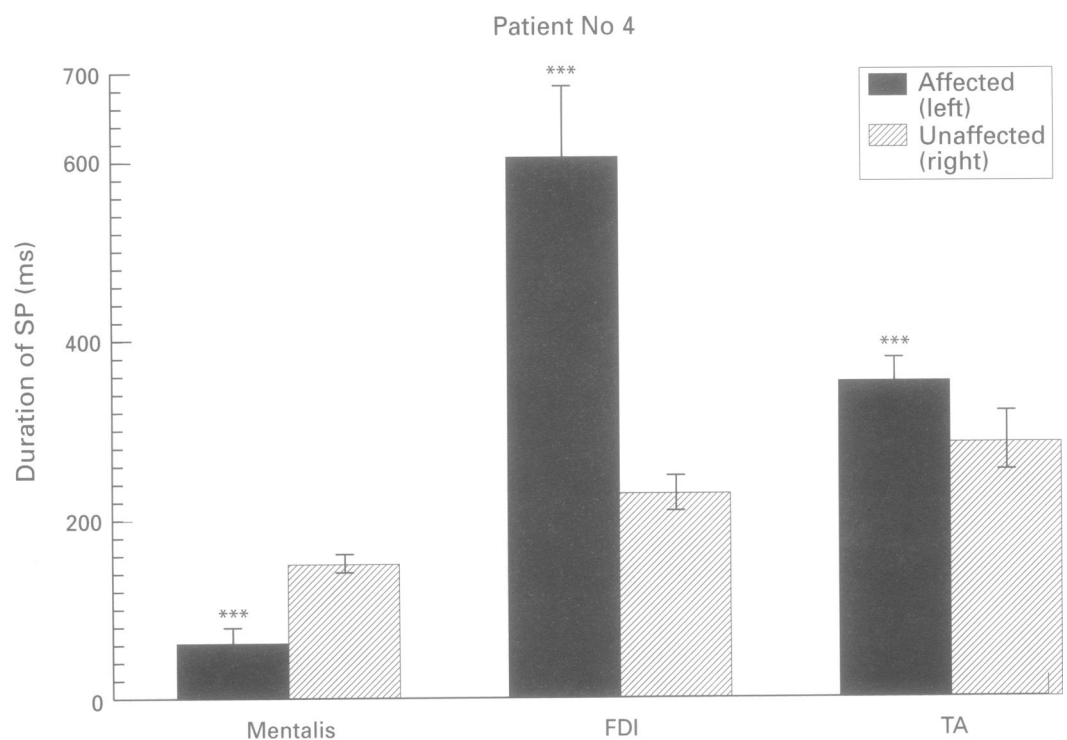
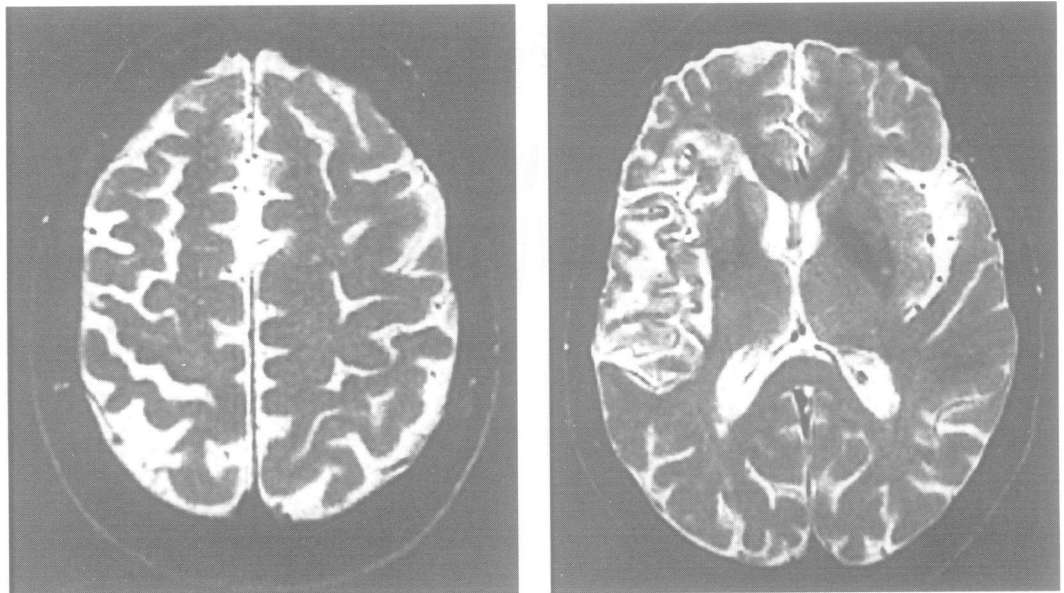
In patient 1 the silent period was prolonged in mentalis muscle with stimulation over the affected compared with the unaffected hemisphere whereas it was shortened in the other eight patients. The absolute latency of the contralateral corticonuclear response in mentalis muscle was normal in all patients, although needle recordings did not always allow a precise estimation of latency.

#### Shortening of the duration of the silent period in facial muscles

In five patients there was evidence of a facial weakness clinically at the time of the study (patients 4 and 6–9) whereas three patients had had only a history of a central facial weakness (2, 3, and 5) and seemed clinically unaffected at the time of the examination. In one patient (2) the facial involvement had been seen at the time when the ischaemic lesion occurred, four months before the study. In the other two patients (3 and 5) facial weakness had been noted as part of a previous transient ischaemic episode (three years and one year respectively) and had resolved completely.

In all patients with either facial weakness at the time of the study or a history of facial involvement the duration of the silent period in mentalis muscle was clearly shorter with stimulation of the affected than the unaffected hemisphere. There was no difference in the amount of shortening of the silent period between the group with clinically evident facial weakness and the group with only a history of facial involvement. An accompanying sensory or motor dysphasia was present in four but not present in three of the patients, and its presence did not influence the amount of shortening of the silent period. Figure 2 shows raw data from patient 6, in (A) illustrating the difference in the duration of the silent period in contralateral muscle after stimulation of the

**Figure 4** Cranial MRI and mean duration of the silent period (SP) in mentalis, first dorsal interosseus (FDI), and tibialis anterior (TA) muscles in patient 6. T2 weighted axial sections of the brain are shown at two different levels illustrating that the medial aspects of the primary motor cortex are preserved while the main pathologically affected area extends laterally involving the face associated primary motor cortex. Bars indicate the SD of silent period duration. \*\*\* $p < 0.001$ .



affected and unaffected hemispheres. By contrast, there was no difference in the duration of the silent period in sternocleidomastoid muscle (fig 2A right panel).

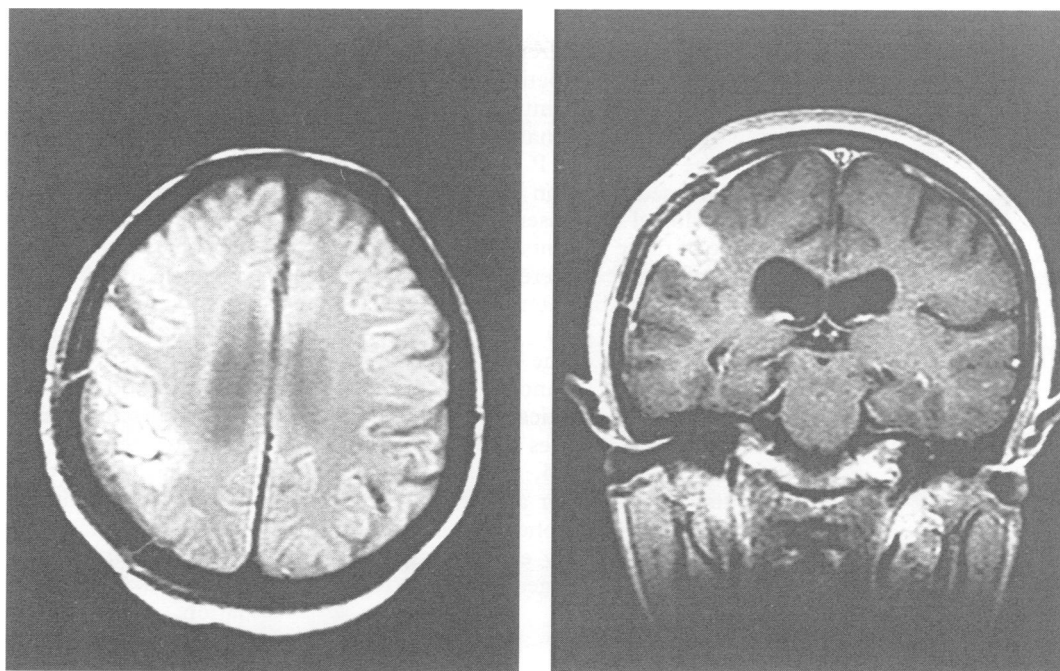
On the basis of MRI or CT there were lesions including the face associated primary motor cortex in all eight patients with shortening of the silent period in mentalis muscle (fig 4).

**COMPARISON OF CONTRALATERAL AND IPSILATERAL RESPONSES IN MENTALIS MUSCLE**  
In the patients with shortening of the silent period in mentalis muscle (except 9 in whom only contralateral muscles were recorded from) silent period duration in both ipsilateral and contralateral muscles was of similar length on both sides—that is, they were long bilaterally with stimulation of the unaffected and short with stimulation of the affected side. This is illustrated in fig 3 and the absolute values of silent period duration in ms are shown

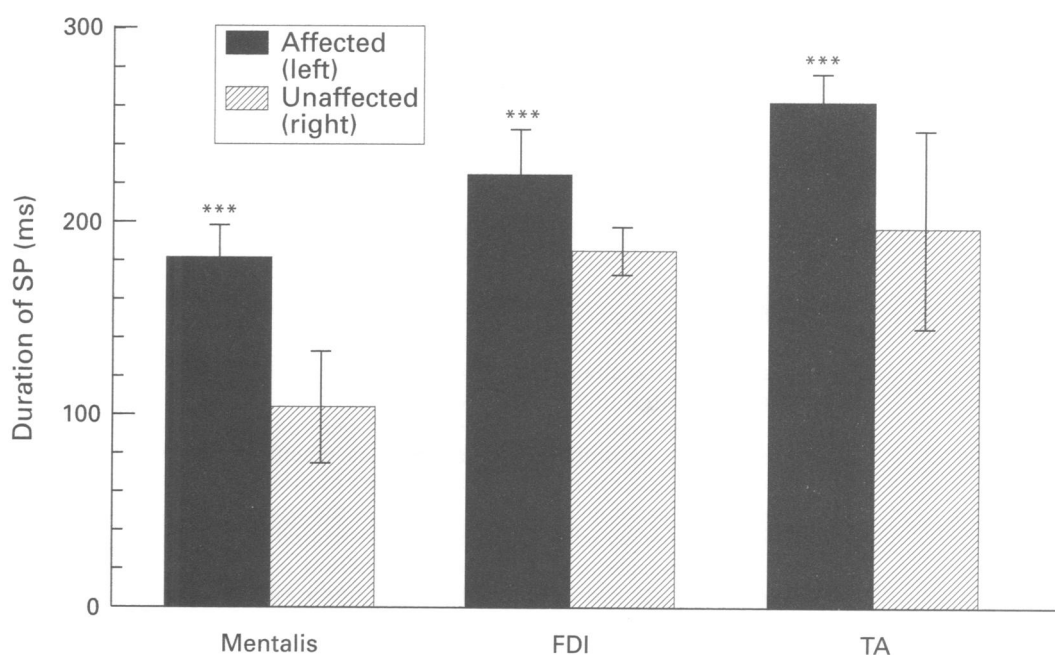
in table 3. Figure 3, illustrating patient 7, shows that the duration of the silent period was abnormally short ipsilaterally and contralaterally with stimulation of the affected hemisphere whereas it was of normal length on both sides when the stimuli were given over the normal hemisphere.

**EFFECTS IN STERNOCLEIDOMASTOID MUSCLE**  
In three patients (6, 7, and 9), in whom recordings were taken from the sternocleidomastoid muscle, there was no interhemispheric difference in the duration of the silent period after stimulation of the two hemispheres. An example illustrating raw data from patient 6 is given in fig 2A and the results are shown in table 3. In patient 7 of table 3 the stimulus intensity was only  $1.2 \times$  threshold, because of the high threshold for responses in sternocleidomastoid muscle in this case. Correspondingly, duration of the silent period

Figure 5 Cranial MRI and mean duration of the silent period (SP) in mentalis, first dorsal interosseus (FDI), and tibialis anterior (TA) muscles in patient 1. T1 weighted axial and coronal sections are shown, illustrating the extent of the right parietal lesion. Bars indicate SD of silent period duration. \*\*\* $p < 0.001$ .



Patient No 1



in this patient was therefore shorter than in the other two. In all patients in whom sternocleidomastoid muscle was recorded from, there was a significant shortening of the silent period in mentalis muscle after stimulation of the affected hemisphere (table 3).

#### PROLONGATION OF SILENT PERIOD DURATION IN FACIAL MUSCLES

Patient 1 had a lesion in the right parietal cortex well outside the primary motor cortex (fig 5). There was no facial palsy. This patient showed a significant prolongation of the silent period with stimulation over the affected hemisphere in all muscles recorded (table 3). This phenomenon was especially pronounced in mentalis muscle (fig 2B, left panel). It should be noted that in this patient, recording

from mentalis muscle, stimulus intensity was  $1.2 \times$  threshold.

#### RECORDINGS FROM FIRST DORSAL INTEROSSEUS AND TIBIALIS ANTERIOR MUSCLES

In six patients (1–4, 8, 9) duration of the silent period in the first dorsal interosseus muscle was significantly prolonged with stimulation of the affected compared with the unaffected hemisphere. One patient (6) did not show either a primary muscle response or a silent period. In the remaining patients there was a shortening of silent period duration in the first dorsal interosseus muscle in one (7) and no significant difference in duration of the silent period between the hemispheres in the other (5). Table 3 summarises the data for silent period measurements in limb muscles.



In tibialis anterior muscle there was an interhemispheric difference of duration of the silent period in four patients (1 and 3–5) with prolongation after stimulation of the affected compared with the unaffected side (mean 61 (9), range 48–67 ms,  $P < 0.001$ ). A concomitant increased duration of the silent period in the first dorsal interosseus muscle was present in three of these patients (1, 3, and 4). Lack of interhemispheric difference of silent period duration in tibialis anterior muscle was noted in three patients (7–9).

Measurements of the central motor conduction time (CMCT) and of the peak to peak amplitude of magnetically evoked potentials (MEP) in limb muscles (table 1) were normal in three patients (1, 4, and 9). The other six patients showed either a decreased amplitude (compared with peripheral electrical stimulation) of the cortically evoked responses or a pathologically prolonged CMCT (for details see table 1).

### Discussion

The present study shows measurements of the silent period evoked by transcranial magnetic stimulation in muscles supplied by cranial nerves in normal control subjects and nine patients with hemispheric brain lesions including the face associated areas of primary motor cortex. The results indicate that not only the long latency corticonuclear responses are present bilaterally after unilateral transcranial magnetic stimulation but also silent periods. In patients with unilateral central facial weakness due to ischaemic lesions of the face associated primary motor cortex, stimulation of the affected hemisphere induced a pathological shortening of the silent period both in the contralateral clinically affected and in the ipsilateral unaffected mentalis muscle. On the other hand, pathologically prolonged silent periods occur both in limb and facial muscles when the lesion lies either outside the primary motor cortex or in only a limited area of primary motor cortex which is not directly associated with the muscle in which the silent period is measured. As discussed below these findings favour a cortical origin of the silent period also in cranial muscles and suggest that this inhibitory action is bilaterally organised, as has been shown for corticonuclear responses induced by transcranial magnetic stimulation.<sup>12</sup>

#### ORIGIN OF THE SILENT PERIOD IN CRANIAL MUSCLES

As in the discussion of the origin of the silent period in limb muscles the question arises as to whether the silent period is induced by segmental interneurons in the medulla or by local inhibitory actions in the primary motor cortex.

In limb muscles spinal motoneuron excitability during the silent period was tested using the H reflex technique and was found to be enhanced or unchanged.<sup>8</sup> Such experiments made a spinal origin of the silent period after transcranial magnetic stimulation unlikely. Furthermore, comparisons between the spinal

inhibition induced by peripheral nerve stimulation, and the silent period after transcranial magnetic stimulation have been performed.<sup>8,17</sup> As far as the silent period in cranial muscles is concerned, similar experiments can hardly be done except in the orbicularis oculi muscle recording the blink reflex. Leis *et al*<sup>18</sup> found a normal excitability of motoneurons innervating the orbicularis oculi muscle during the silent period induced by transcranial magnetic stimulation as tested by modulation of the R1 component of the blink reflex. Peripheral stimulation of the facial nerve is followed by a silent period which is much shorter than that after transcranial magnetic stimulation.<sup>6,9</sup> This finding, however, does not really exclude a medullary origin of the silent period after transcranial magnetic stimulation as it cannot be ruled out that corticonuclear fibres excite medullary inhibitory interneurons which are not recruited by peripheral facial nerve stimulation.

In the patients, the duration of the silent period was pathologically shortened in eight out of nine patients (2–9) with stimulation of the affected compared with the unaffected hemisphere both in the contralateral clinically affected and in the ipsilateral unaffected mentalis muscle (fig 3). In all patients with silent period shortening in mentalis muscle there was a central facial weakness clinically either at the time of the study or on the basis of the patient's history. Furthermore, the face associated primary motor cortex was affected according to CT and MRI (fig 4). Only recently, von Giesen and coworkers,<sup>14</sup> analysing 30 patients with lesions of different brain areas, showed that the duration of the silent period depends on whether the primary motor cortex is directly involved in the lesion or whether there is damage to areas projecting to the primary motor cortex (for example, thalamus, supplementary motor cortex). Patients with the former type of lesion showed a shortening of the silent period in limb muscles. Similar to their conclusion we therefore suggest that a shortening of the silent period in the patients is due to direct damage to inhibitory intracortical interneurons, which are considered to generate the silent period.

#### BILATERAL CORTICAL ORGANISATION OF CRANIAL MUSCLES

Cranial motor nuclei receive bilateral cortical input via corticonuclear fibres.<sup>19</sup> Bilateral EMG responses could be recorded from orbicularis oris, orbicularis oculi, mentalis, sternocleidomastoid, masseter, and tongue muscles with a delay compatible with excitation of corticonuclear pathways.<sup>12,20,21</sup>

The present investigation shows that after stimulation of the primary motor cortex projecting to cranial nuclei, in addition to bilateral corticonuclear responses, silent periods in the contralateral and ipsilateral cranial muscles occur. In mentalis muscle the duration is somewhat longer in the contralateral than the ipsilateral side.

It could be argued that the occurrence of a bilateral silent period is not compatible with a

cortical origin. Taken for granted that tonic activity in cranial muscles results from both excitation of the contralateral and ipsilateral primary motor cortex it may be surprising that a silent period in ipsilateral muscles after unilateral transcranial magnetic stimulation occurs at all. If the silent period originates from intracortical inhibitory interneurons the excitatory drive of the stimulated hemisphere should be reduced, leaving the excitatory drive of the other non-stimulated hemisphere innervating ipsilateral muscles uninfluenced. The inhibitory drive generated by transcranial magnetic stimulation to one hemisphere may reduce the net excitation at the motoneuronal level so that for some motoneurons the remaining excitation from the other hemisphere may not be sufficient to reach firing threshold. If this is the case, the ipsilateral silent period would be expected to be incomplete. Indeed, inspection of original recordings (see also fig 1) indicates that EMG activity is not decreased to zero during the silent period, but rather in most cases a low level of EMG activity persists. As both the duration and the intensity (the reduction of the remaining EMG activity) of the silent period is more pronounced in contralateral than in ipsilateral muscles especially in mentalis and genioglossus muscle (fig 1), the contralateral hemisphere apparently has a stronger influence on motoneuron activation than the ipsilateral one. By contrast, in sternocleidomastoid muscle the ipsilaterally and contralaterally induced silent period seems to be of similar duration and intensity—that is, both hemispheres have equal influence. This is in line with the clinical finding that—for example, in acute stroke—a contralateral paresis occurs in lower facial and tongue muscles but not in sternocleidomastoid muscle.

#### PROLONGATION OF THE SILENT PERIOD IN FACIAL AND LIMB MUSCLES

In patient 1 the duration of the silent period was pathologically prolonged with stimulation of the affected compared with the unaffected hemisphere (table 3, figs 2 and 5). Furthermore, silent periods in the first dorsal interosseus and tibialis anterior in this patient were also prolonged with stimulation over the affected hemisphere compared with the unaffected one (table 3). One may argue that the duration of the silent period in mentalis muscle on the unaffected side was abnormally short compared with the controls. It should be noted, however, that firstly in this patient a stimulus intensity of only  $1.2 \times$  threshold (72% of the maximum output of the device) was used when recording from mentalis muscle. Secondly, on statistical grounds (*t* test) this difference reached a *P* value of only 0.017 compared with normal on the unaffected side whereas the *P* value for the affected side was  $< 0.001$ . In this patient MRI showed a right parietal lesion due to resection of a haemangioma and no abnormalities in the left hemisphere (fig 5). Clinically there were no motor but only sensory deficits affecting the left arm. For this reason we consider the duration of the

silent period in the left mentalis muscle stimulating over the right affected hemisphere abnormally long compared with the contralateral duration.

As has been shown by von Giesen *et al*<sup>14</sup> in limb muscles, a pathologically prolonged silent period may occur if there is damage to areas projecting to the motor cortex (thalamus, parietal cortex). Other studies have also highlighted the influence of corticocortical connections on the excitability of primary motor cortex.<sup>22,23</sup> Although one has to interpret the results in this patient only tentatively until further supportive data are obtained, the prolongation of the silent period in this patient may be due to disfacilitation of the primary motor cortex caused by a lack of afferent cortical input from the parietal cortex as already proposed by von Giesen *et al*.<sup>14</sup>

As opposed to facial muscles, the dominant finding in limb muscles in the remaining patients was also a significant prolongation of the silent period (table 3). The question arises as to why such a uniform prolongation occurs. A common denominator may be that all such patients presented with a central facial weakness and had a dominant lesion to the face associated primary motor cortex. Face associated areas of primary motor cortex project to the limb associated primary motor cortex via corticocortical connections and may therefore influence the activity of the pyramidal cells and local interneurons of these primary areas of the motor cortex. Synaptic contacts with pyramidal cells and with excitatory or inhibitory interneurons are made by corticocortical fibres in the superficial layer of primary motor cortex as has been shown by electron microscopy.<sup>24-26</sup> The prolongation of the silent period durations in limb muscles in the patients with a dominant lesion of the face associated area of primary motor cortex and a corresponding shortening of the silent period in mentalis muscle may therefore be caused by deafferentation due to lesions of corticocortical afferents from the face area to the arm or leg area of the primary motor cortex. The presence of pyramidal signs in the limbs (table 1) does not, therefore, always imply shortening of the silent period as there was prolongation of the silent period in limb muscles even with pyramidal signs clinically in some patients as has been shown previously.<sup>10,14</sup>

In summary our data in normal subjects show that there is a bilateral silent period in tonically active muscles supplied by cranial nerves after unilateral magnetic stimulation. The findings cannot conclusively prove a cortical origin of the silent period. The experiments in normal subjects and the results in patients, however, strongly suggest that the silent period results from local inhibitory actions in the primary motor cortex. In patients, changes in silent period duration in different muscles seem to depend on the area primarily involved in the lesion. Stimulation of the "epicentre" of a lesion in the motor cortex, where direct damage to the pyramidal cells and surrounding interneurons occurred, seems to give rise to a shortening of the silent period in related

muscles. By contrast, the lack of corticocortical projections from the centre of the lesion to adjacent areas may lead to an increase in silent period duration in muscles supplied by these adjacent motor cortical regions. Further studies must concentrate on serial observations of variables reflecting influences between different motor cortical areas to better understand the pattern of functional reorganisation of the brain after structural damage. The silent period after transcranial magnetic stimulation in different muscles as an easily obtainable variable may hereby be useful.

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