Increased Sensitivity to Ipsilateral Cutaneous Stimuli Following Transcranial Magnetic Stimulation of the Parietal Lobe

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Transcranial magnetic stimulation of the sensorimotor cortex results in decreased sensitivity of threshold electrical stimuli to fingers of the contralateral hand. It has been suggested that one factor contributing to neglect contralateral to a unilateral parietal lesion is a release of the normal hemisphere from reciprocal interhemispheric inhibition by the damaged hemisphere. Consistent with this account, the current study demonstrated that transcranial magnetic stimulation over the parietal cortex results in increased sensitivity to cutaneous stimulation ipsilateral to the stimulation. The likely mechanism is a transcranial magnetic stimulation–induced transient dysfunction of the ipsilateral parietal cortex that then results in disinhibition of the contralateral parietal cortex.

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Cohen and colleagues [1] proposed that the phenomenon of extinction can be explained by interhemispheric rivalry in which each parietal lobe inhibits the orienting bias of its partner [2, 3]. This account of the pathophysiology of parietal neglect postulates that parietal lesions will cause not only a deficiency of contralesional orienting, but also a hyperorienting in the ipsilesional direction. Recent experimental studies of patients with neglect afforded some evidence of ipsilesional hyperorienting [4–6].

Transcranial magnetic stimulation (TMS) causes a transient disruption of normal cortical function subja-

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cent to the stimulation [7, 8]. We sought evidence, using TMS in normal subjects, that the parietal lobe inhibits the opposite hemisphere, and that this inhibition influences perceptual processing by the opposite hemisphere. The experiments in this study measured the effects of transient inactivation of parietal cortex on ipsilateral tactile thresholds.

Materials and Methods

TMS was performed using a Cadwell MES-10 stimulator with a figure-8–shaped coil. The diameter of each component of the coil measured 4.5 cm, and at maximum intensity the coil produced a magnetic flux of approximately 2.0 T.

Two ring electrodes were placed around the right thumb. Current pulses, having a duration of 0.3 msec, were delivered to these electrodes using a Grass stimulator and a constant-current stimulus isolation unit.

All subjects were right-handed and underwent TMS over the right hemisphere. The coil position was adjusted over the sensorimotor cortex until a site was determined at which the lowest possible output of the MES-10 resulted in visible contraction of the left hand. The output of the MEW-10 was then increased to approximately 10% above that value and maintained at that level for the duration of the experiment. The range of intensities was between 85 and 100% of maximum output of the MES-10.

Experiment 1

Five neurologically healthy subjects (2 men) were studied. The age range was 18 to 30 years. All subjects participated after giving informed consent.

For each block of trials, starting with suprathreshold stimuli, the stimulus intensity of the current pulse was gradually decreased until the percentage of stimuli correctly identified by the subject fell to less than 50% of all stimuli.

Paired stimuli (magnetic pulse followed 50 msec later by the current stimulus to the thumb) were delivered in sets of 20 stimulus pairs. Following each stimulus pair, the subjects were instructed to respond with a "yes" or "no" even when they were uncertain about whether the stimulus to the thumb was perceived. The interpulse interval of 50 msec was chosen because at this interval, TMS maximally suppresses cutaneous perception in the fingers of the contralateral hand [7].

Responses to sets of 20 stimulus pairs were determined with the midpoint of the coil located 3 cm anterior to the sensorimotor cortex (frontal condition), and 1, 3, and 5 cm posterior to the sensorimotor cortex (parietal condition). These locations were on the coronal plane passing through the sensorimotor cortex as defined previously. A set of responses at each of these sites was initially obtained. The parietal site with the largest number of correct responses was determined. Subsequently, one additional set of responses was obtained with the coil position alternating between the frontal and the parietal so that a total of 40 responses from each of the 5 subjects was obtained at each site.

Experiment 2

The stimulus current to the ring electrodes was gradually increased to the level at which each subject could first correctly identify all cutaneous stimuli delivered to the thumb (100%). The stimulus intensity was then gradually decreased until the subject could not perceive any of the stimuli delivered to the thumb (0%). Three intermediate stimulus current settings at 25, 50, and 75% were determined for each subject. Five subjects (only one of whom had participated in experiment 1) were studied.

Responses to sets of stimulus pairs (magnetic pulse followed by cutaneous stimulus to the thumb) were obtained with the coil at 5 cm anterior to the sensorimotor cortex (frontal condition), at the sensorimotor cortex (SM condition), and at 3 cm (Par3 condition) and 5 cm (Par5 condition) posterior to the sensorimotor cortex. At each site, a stimulus intensity-response curve was obtained for each subject by recording responses to stimuli at each of the five current intensities. The current pulse intensity was randomized within a given block of trials. The intensity of the magnetic pulse was determined as in experiment 1 and maintained at that level for the duration of the experiment.

A two-way analysis of variance (ANOVA), with TMS location and current pulse intensity as the two within-subject factors, was used to analyze the data. Appropriate planned comparisons were then applied to identify the source of interactions. The nonparametric Friedman repeated measures ANOVA on ranks was applied to the data obtained at the four sites.

Results

Experiment 1

For each subject, more stimuli were perceived following parietal TMS as compared to stimuli delivered following frontal TMS (Table 1). Following frontal TMS, 22% of ipsilateral thumb stimuli were perceived (standard deviation, 21). Following parietal TMS, however, 50% of stimuli were perceived (standard deviation, 20). The data passed the Kolomorogov-Smirnov normality test. The paired t test showed that the difference between the two TMS locations was statistically significant ($t = 7.1$; $p = 0.002$). The difference between the stimuli perceived after electrical stimulation without TMS as compared to electrical stimulation following frontal TMS was not significant ($p = 0.4$).

Experiment 2

The stimulus response curves at the four TMS sites are plotted in the Figure. The site of TMS significantly influenced sensory threshold ($F[3, 12] = 5.56$, $p < 0.013$). TMS location interacted with stimulus intensity ($F[12, 48] = 2.282$, $p < 0.025$).

Planned comparisons of the Par3, Par5, and SM conditions with the frontal TMS condition were made (Table 2). Sensory thresholds when stimulating ipsilaterally over Par3 were significantly lower than those obtained from the frontal TMS condition ($F[1, 4] = 8.42$, $p < 0.05$). There was a lower sensory threshold when stimulating over Par5 than in the frontal TMS

Table 1. Percent Detection in Each Subject with No Transcranial Magnetic Stimulation (TMS) and with TMS Applied over the Frontal and Parietal Scalp

Subject No.	No TMS	Frontal	Parietal
1	10	8	40
2	15	38	53
3	8	0	40
4	15	13	38
5	30	50	80
Mean	16	22	50
Standard error of mean	4	10	8

Table 2. Transcranial Magnetic Stimulation (TMS) over the Frontal Cortex, Sensorimotor Cortex (SM), and at 3 cm (Par3) and 5 cm (Par5) Posterior to the Sensorimotor Cortex

Subject No.	Frontal TMS	SM	Par3	Par5
1	62	56	72	74
6	30	36	34	44
7	40	46	50	48
8	50	48	50	50
9	34	34	50	46
Mean	43	44	52	52
Standard error of mean	6	4	5	5

condition ($F[1, 4] = 10.565$, $p < 0.04$). Responses obtained with the coil located over the sensorimotor cortex did not differ from those obtained after frontal stimulation ($F < 1$).

The Friedman test confirmed that the stimulus response curves at the four sites were significantly different ($p = 0.0016$). Dunnet's test (multiple comparisons vs the frontal control group) confirmed that the Par3 and Par5 conditions were significantly different from the frontal TMS condition ($p < 0.05$).

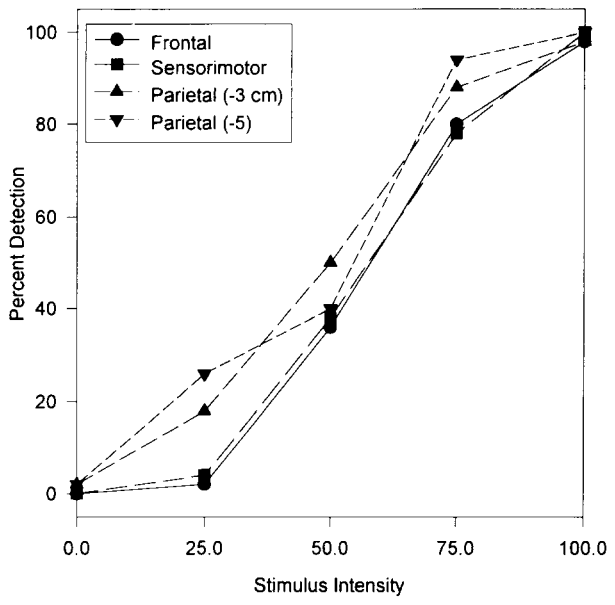
Discussion

It has been proposed that extinction results when the normal hemisphere inhibits the damaged hemisphere more than the damaged hemisphere inhibits the normal one [2, 3, 9, 10]. Heilman and coauthors [11] postulated a reciprocal gating mechanism involving the nucleus reticularis (NR) of the thalamus. The NR normally inhibits sensory transmission to the ipsilateral cortex. Each association cortex inhibits the ipsilateral NR, decreasing inhibition of ipsilateral sensory input, and simultaneously facilitates the contralateral NR, gating out sensory input to the contralateral cortex. A lesion of the association cortex should then make the contralateral cortex more sensitive to sensory stimuli.

The current investigation provides direct evidence for this hypothesis. Transient parietal inactivation by TMS was shown to decrease ipsilateral sensory thresholds. This phenomenon of enhancement of cutaneous perception elicited by TMS was localized. It was not elicited by TMS over the frontal cortex or the sensorimotor cortex. The effect is maximal when TMS is localized 3 to 5 cm posterior to the sensorimotor cortex. This region overlies association cortex. The specificity of association cortex stimulation, and not sensorimotor cortex stimulation, in producing disinhibition of sensory detection is a new finding.

Other mechanisms that may account for our findings include TMS-induced disinhibition of afferent transmission during the ipsilateral silent period [12, 13] and TMS-induced sudomotor response [14]. These TMS-induced effects, however, do not occur outside the sensorimotor cortex. TMS-induced increase in excitability of neurons in the contralateral primary sensory cortex, analogous to that suggested for TMS of the motor cortex [15], has not been demonstrated. We conclude that enhancement of perception of ipsilateral cutaneous stimuli delivered at a time when the function of the ipsilateral association cortex was transiently disrupted by TMS provides support for the reciprocal inhibition model.

Each point represents the mean in 5 subjects. The abscissa is the stimulus intensity. The ordinate is percent detection of stimuli to the ipsilateral thumb.



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