

Feeling by Sight or Seeing by Touch?

Lotfi Merabet,¹ Gregor Thut,¹ Brian Murray,¹
Jessica Andrews,¹ Steven Hsiao,²
and Alvaro Pascual-Leone^{1,*}

¹Laboratory for Magnetic Brain Stimulation
Beth Israel Deaconess Medical Center
Harvard Medical School
330 Brookline Avenue
Boston, Massachusetts 02215

²Zanvyl Krieger Mind/Brain Institute
Johns Hopkins University
3400 North Charles Street
Baltimore, Maryland 21218

Summary

We have addressed the role of occipital and somatosensory cortex in a tactile discrimination task. Sighted and congenitally blind subjects rated the roughness and distance spacing for a series of raised dot patterns. When judging roughness, intermediate dot spacings were perceived as being the most rough, while distance judgments generated a linear relation. Low-frequency rTMS applied to somatosensory cortex disrupted roughness without affecting distance judgments, while rTMS to occipital cortex disrupted distance but not roughness judgments. We also tested an early blind patient with bilateral occipital cortex damage. Her performance on the roughness determination task was normal; however, she was greatly impaired with distance judgments. The findings suggest a double-dissociation effect in which roughness and distance are primarily processed in somatosensory and occipital cortex, respectively. The differential effect of rTMS on task performance and corroborative clinical evidence suggest that occipital cortex is engaged in tactile tasks requiring fine spatial discrimination.

Introduction

We acquire sensory representations from different specialized modalities (e.g., vision, touch, and hearing), yet our perception of the world is highly integrated and unitary. Despite their independent capture, it is clear that information from one sense influences the perception obtained from another. The classical view in neurophysiology purports that early sensory processing is carried out in parallel and in a strict modality-specific manner. Sensory integration is subsequently achieved within specialized multimodal associative areas (Stein and Meredith, 1993). Emerging evidence has forced us to reevaluate this view, given that processing of one sensory modality can recruit primary cortical regions typically reserved for a different modality. For example, in early blind individuals, occipital cortical areas (normally implicated in visual perception) are active during tactile

and auditory tasks (Sadato et al., 1996, 2002; Buchel et al., 1998; Burton et al., 2002; Roder et al., 2002). Furthermore, activation of occipital cortex appears to be functionally relevant for tactile Braille reading (Cohen et al., 1997; Hamilton et al., 2000). Such examples of cross-modal processing are not limited to sensory deprived conditions. Studies in sighted subjects have demonstrated that occipital cortical areas are also implicated in the processing of nonvisual information (Sathian et al., 1997; Deibert et al., 1999; Zangaladze et al., 1999; Amedi et al., 2002).

Assessing surface texture requires sensory integration from a variety of sources (Lederman, 1982). The roughness and distance between elements of a texture pattern are important cues that add sensory information for vision as well as touch and might be viewed as “microgeometric” and “macrogeometric” cues, respectively (Roland et al., 1998). Neuroimaging data has suggested that there may exist a functional separation in cortical processing of micro- and macrogeometric cues (Roland et al., 1998). Furthermore, it has been suggested that the contribution one sense makes over another depends on the nature of the task. Specifically, vision may be better suited for tasks determining the “spatial density” of textures, while touch may be more appropriate for tasks requiring the judgment of roughness (Guest and Spence, 2003). We hypothesized that disrupting somatosensory cortex would preferentially impair subjective microgeometric (i.e., roughness) judgments, while disruption of occipital cortex would preferentially impair macrogeometric tasks requiring fine graded spatial judgment (i.e., distance). To test this hypothesis, we assessed the psychophysical performance of sighted individuals on a tactile task (using arrays of raised dot patterns) prior to and following rTMS to these areas using an offline experimental approach (i.e., task performance was assessed prior to and immediately after stimulation) (Figure 1). Repetitive TMS has been widely used to disrupt cortical function (reversibly and noninvasively) in a given brain area in order to investigate its functional role by observing the behavioral consequences of its inactivation (Pascual-Leone et al., 2000; Robertson et al., 2003).

Finally, we have sought corroborative evidence by comparing psychophysical performance in congenitally blind subjects with an early blind patient who became alexic for Braille following a bilateral occipital stroke (Hamilton et al., 2000). Given the incurred damage to her occipital cortex and lack of prior visual experience, we hypothesized that her performance would be selectively impaired in tactile tasks requiring fine spatial judgments.

Results

Performance in Sighted Subjects

Psychophysical performance on the roughness versus distance judgment task was similar to previous reports (Connor et al., 1990; Johnson and Hsiao, 1992). Figure

*Correspondence: ap Leone@caregroup.harvard.edu

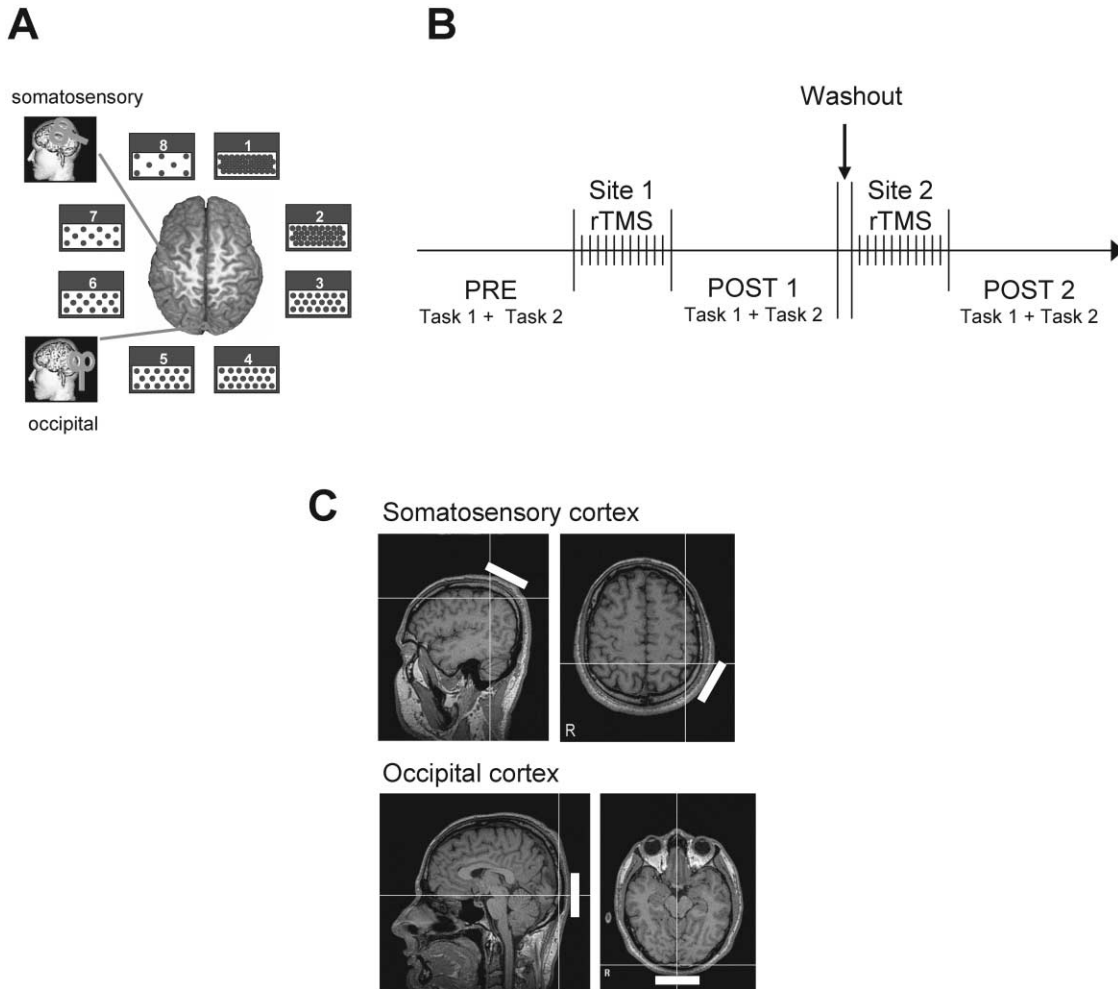


Figure 1. Experimental Methodology

(A) Tactile stimuli used in this study. Eight raised dot patterns of varying interdot spacing used for judgment of roughness and distance. rTMS was applied to either somatosensory or occipital cortex.

(B) Time line of behavioral task.

(C) Estimated site of stimulation in somatosensory and occipital cortex shown in one subject (line intersection) with position of the TMS coil (white bar). Stimulation sites were verified a posteriori using the subject's own MRI coregistered with a frameless stereotaxic guidance system (Brainsight, Montreal, Canada).

2 illustrates these results. When judging roughness, intermediate dot spacing was perceived as the most subjectively rough, while closely and widely spaced dot patterns felt smoother. Therefore, plotting subjective perceived roughness against actual dot spacing yielded an inverted U-shape curve (Figure 2A; black symbols) with a maximal value corresponding to a dot spacing of 3 mm. On the other hand, subjective distance judgments plotted against actual dot spacing generated a linear relation (i.e., greater interdot spacings were systematically perceived as greater distances) (Figure 2B; black symbols).

Effect of rTMS on Task Performance

We applied rTMS to either somatosensory or occipital cortex in order to uncover the functional contribution of each area in this tactile task. Following rTMS to the contralateral somatosensory cortex, we found a disrupt-

tion of roughness judgment with a global dampening of the subjective reports (Figure 2A; light gray symbols). While subjects still perceived the 3 mm spacing as the interdot spacing generating the maximal impression of roughness, the magnitude of the perceived roughness was significantly suppressed [TMS main effect: $F(2,20) = 11.3$, $p = 0.0005$; Scheffé: S1 versus PRE, $p = 0.002$; S1 versus V1, $p = 0.003$]. This result fits with observations during postexperiment debriefing in which subjects reported that the arrays “did not feel as bumpy” or “were less sharp” following somatosensory cortex stimulation. In contrast, rTMS application to the occipital cortex did not affect roughness judgment at all (Figure 2A, dark gray symbols; Scheffé: V1 versus PRE, $p = 0.99$). The opposite effect was found for distance judgment [TMS main effect: $F(2,20) = 6.7$, $p = 0.006$]. In this case, subjective judgments were impaired by occipital stimulation (Figure 2B, dark gray symbols; Scheffé: V1 versus PRE,

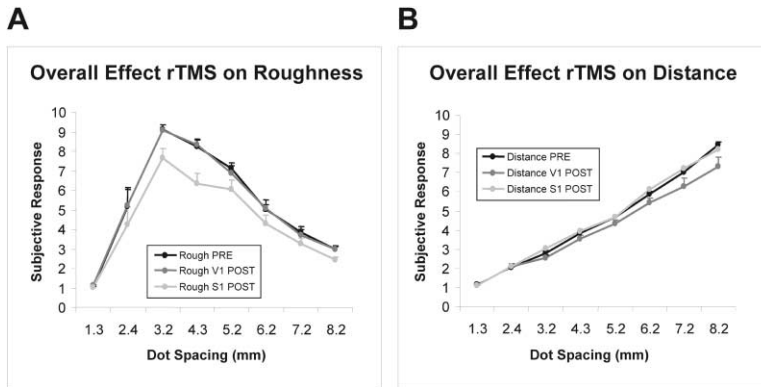


Figure 2. Mean Performance of Sighted Subjects for the Tactile Task

Subject's baseline responses for roughness (A) and distance (B) determination are plotted against dot spacing (black symbols). (A) Effect on roughness determination. Note an overall dampening of the roughness judgment curve following somatosensory cortex disruption (light gray symbols) but not occipital cortex (dark gray symbols). (B) Effect on distance determination. Disruption of occipital cortex impaired distance perception at increasing dot spacing (dark gray symbols) but had no effect following somatosensory cortex disruption (light gray symbols). Error bars represent standard error (SE).

$p = 0.03$; V1 versus S1, $p = 0.01$) but not by stimulation of somatosensory cortex (Figure 2B, light gray symbols; Scheffé: S1 versus PRE, $p = 0.86$). Specifically, subjects tended to report less of an interdot distance with increasing spacing.

TMS effects depended on interdot spacing for both roughness and distance judgments [interaction TMS \times Tactile pattern: both $F(14,140) > 3.5$, $p < 0.00006$]. The disruptive effect was most evident at the intermediate interdot spacing of 4.3 mm for roughness judgment (Scheffé: S1 versus PRE, $p = 0.003$; S1 versus V1, $p = 0.004$) and at the largest interdot spacing of 8.2 mm for distance judgments (Scheffé: V1 versus PRE, $p = 0.006$; V1 versus S1, $p = 0.03$).

Control stimulation over the vertex did not reveal any significant main effect of TMS (PRE versus Vertex) or any significant interaction with dot spacing for either roughness or distance judgments (TMS: all $F < 1$, n.s.; TMS \times Tactile Pattern: all $F < 1.7$, $p > 0.13$).

Task Performance in Blind Patients

Further support for the role of occipital cortex in fine tactile judgments was obtained from an early-blind patient with alexia for Braille following a bilateral occipital stroke. Though rendered unable to read Braille, she was able to correctly discriminate between texture patterns and identify everyday objects by touch (e.g., coins and keys). Her performance on the roughness task was within the range of responses reported by the sighted and congenitally blind controls for all dot spacings. An inverted U-shaped function and maximal roughness centered at the 3 mm was observed falling within the maxima and minima of sighted and early blind controls (Figure 3A). However, her performance on distance judgments was greatly impaired, characterized by a global flattening of the curve at almost all interdot spacings tested (Figure 3B). Her deviance from both the sighted and congenitally blind groups for distance judgments was evident at pattern spacings of 5.2 mm and greater. Performance of congenitally blind subjects was similar to sighted controls for both the roughness and distance tasks (no significant difference between groups, all $F < 2.6$, $p > 0.13$).

Discussion

Our findings suggest that the occipital (visual) cortex is functionally involved in tactile information processing in

normally sighted individuals. Specifically, its role appears to be related to tactile tasks requiring fine spatial judgments. Low-frequency (1 Hz) rTMS applied to somatosensory or occipital cortex selectively interfered with tactile performance in a behaviorally relevant and functional manner. Transient disruption of visual cortical areas using rTMS did not hinder texture (roughness) judgments but impaired the subject's ability to judge the relative distance spacing between raised dot patterns. Conversely, transient disruption of somatosensory cortex impaired roughness judgments (flattening the overall impression of roughness of the tactile stimuli), while interdot distance judgments remained intact. These results demonstrate a functional resolution between two distinct tactile tasks and two different cortical sites and further suggest that occipital and somatosensory cortex contribute differently to behavioral performance.

Corroborative evidence that visual cortex is implicated in fine spatial texture judgment was obtained by testing an early-blind patient who suffered a bilateral occipital ischemic stroke. This patient's texture judgments of roughness were intact and comparable to normally sighted and congenitally blind subjects' performance. However, her ability to carry out distance judgments was significantly impaired. Though we did not have the opportunity to test her baseline performance before the acute neurological event, her psychophysical performance is in agreement with the data obtained following occipital rTMS in sighted subjects.

The disruptive effect on roughness determination was greater than that for distance. This is most likely related to the fact that the tasks are fundamentally different and therefore may well recruit different neural mechanisms. However, several methodological considerations are important. First, the occipital cortical areas implicated in these tactile determinations are likely to include regions beyond the disrupted activity induced by TMS as applied in the present study. Neuroimaging studies investigating the neural correlates implicated with roughness-distance determinations are likely to assist in resolving this issue. Second, while TMS intensity of 110% motor threshold has been demonstrated to depress excitability in sensorimotor cortex, it may not be sufficient to depress excitability in occipital cortex. Indeed, it has been reported that motor threshold (measured from motor cortex) and phosphene threshold (measured from occipital cortex) are not correlated within the same subject (Borojerdi et al., 2002), and thus in some cases, we

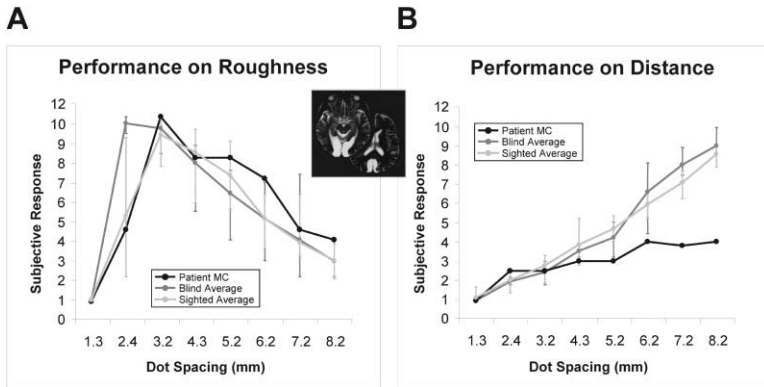


Figure 3. Performance of a Congenitally Blind and Braille Alexic Patient

Inset figure: T_2 -weighted MRI scan showing bilateral damage to primary visual cortical areas. For complete case report, see Hamilton et al. (2000). Performance is compared to the group average of normal sighted controls and congenitally blind subjects (error bars represent scored maxima and minima at each dot spacing).

(A) Performance on roughness task (black symbols) compared to baseline sighted group (light gray symbols) and congenitally blind (dark gray symbols) averages.

(B) Performance on distance task (black symbols) compared to baseline sighted group (light gray symbols) and congenitally blind

(dark gray symbols) average. Note that patient MC's roughness perception falls within the ranges of both sighted and congenitally blind subjects while her distance judgments are impaired particularly at greater dot spacing compared to both these groups.

may have been applying TMS at an intensity that did not disrupt occipital cortex optimally. A dose-response procedure where the effect of different stimulation intensities on behavior is assessed may help to clarify this issue.

Our paradigm takes advantage of the fact that tactile roughness and distance spacing determinations can be dissociated by psychophysical performance (an inverted U profile for roughness and a monotonic relation for distance judgment; see Connor et al., 1990). It is important to note that such a dissociation has not always been observed. Specifically, Meftah et al. (2002) have reported a monotonic increase in perceived roughness with increasing spacing. As the authors suggest, this discrepancy may be related to the physical characteristics of the tactile stimuli used (e.g., height of tactile dots) and the mode of presentation (passive versus active touch; see Meftah et al., 2002). It is possible that a different effect on performance following rTMS application would result if subjects explored the tactile stimuli used by the aforementioned group. This issue merits further study and may provide for interesting and contrasting findings.

Previous studies have demonstrated activation of occipital cortex during tactile tasks in blind and sighted subjects (Sadato et al., 1996, 2002; Buchel et al., 1998; Burton et al., 2002; Sathian et al., 1997; Deibert et al., 1999; Amedi et al., 2002). Taken together, these findings suggest that tactile object processing incorporates a complex network implicating visual and haptic cortical areas sharing common representations. Furthermore, feedback projections from parietal areas may provide the neural substrate as to how both these senses interact with each other (Macaluso et al., 2000). The functional significance of occipital activation in tactile tasks has been previously assessed using TMS. In early blind subjects, Cohen et al. (1997) found that TMS applied to occipital cortex disrupted Braille letter reading. Interestingly, subjects knew that they were touching Braille symbols but were unable to discriminate them, suggesting that this area was implicated in the actual identification of letters rather than simple tactile detection. In sighted individuals, Sathian and coworkers (1997) employed a gratings orientation task (GOT) and PET imaging to demonstrate that tactile discrimination leads to increased

metabolic activity within left parieto-occipital cortex. In a follow-up study, Zangaladze and coworkers (1999) used TMS to show that interference with cortical processing in this parieto-occipital area selectively impaired orientation discrimination but not spacing judgments. Furthermore, disruption of somatosensory cortex impaired discrimination performance on both orientation and spacing tasks (Zangaladze et al., 1999). These results may appear discrepant to the findings reported here. However, there are several important aspects that differentiate these two studies and we believe render these results complementary, rather than contradictory. First, Zangaladze et al. (1999) used gratings with a fixed spacing (3 mm for most test subjects). In our study, tetragonal-arranged raised dot arrays (having no overall orientation relative to the finger axis) with spacing varying from 1 to 8.2 mm were used. Thus, in our study, the subjects were asked to explore a much broader range of interdot spacings. As revealed in Figure 2 of our results, had we limited ourselves to a spacing of 3 mm, we would have failed to observe an effect on distance judgments following rTMS application to the occipital cortex. Second, participants in our study actively explored the tactile patterns (lasting approximately 2 s) and were asked to subjectively rate overall roughness and distance using a 1–10 scale. Zangaladze et al. (1999) presented their gratings for 63 ms to the immobile finger of their subjects who were asked to perform a two-alternative forced choice task (orientation alignment with respect to finger and “narrow” versus “wide” groove spacing). Active exploration of the tactile stimuli, time of exposure, and a forced choice versus subjective rating paradigm may all influence the neural structures implicated in the task and hence condition the results. Third, the site of occipital stimulation (and thus the cortical region primarily disrupted) was different between the two studies. In the Zangaladze study, the investigators targeted a region near the contralateral parieto-occipital fissure previously identified by the same investigators to be active during their specific tactile task (Sathian et al., 1997). It is not clear if this same area is active while performing the tactile task employed in our study. We targeted the occipital cortex bilaterally (likely disrupting VI and V2) with the rationale that distance determination would necessitate fine spatial judgments and thus impli-

cate early cortical regions with well-developed retinotopic representations. Finally, we delivered repetitive TMS using offline stimulation (i.e., applied between task performance) while Zangaladze et al. (1999) delivered single-pulse TMS following an online design. The advantage of using an offline paradigm is that this approach avoids the nonspecific effects associated with TMS stimulation (such as somatic sensations and attention-related effects; see Robertson et al., 2003).

Work from other groups has suggested that visual imagery is an obligatory component of spatial discrimination, facilitating tactile shape discrimination or object recognition via top-down activation of visual representations (Sathian et al., 1997; Zangaladze et al., 1999). Although this possibility cannot be completely ruled out, our findings suggest that visual imagery cannot be the sole factor. First, none of the subjects were allowed to see the tactile stimuli used in the study and thus could not make determinations based on prior visual recollection. Second, congenitally blind subjects exhibited performance similar to that of sighted controls on both the roughness and distance tasks. The fact that individuals in this group were all profoundly blind (and thus possess minimal memory from prior visual experience) suggests that visual imagery is not necessary to carry out these tasks. Finally, though we do not have psychophysical data on patient MC prior to her acute neurological event, it is clear from her performance that she had great selective difficulty with the distance determination task while her roughness judgments remained intact. This strongly points to the implication of occipital cortex in performing tasks requiring fine spatial judgment. As with congenitally blind subjects, it is unlikely that her impairment in the distance judgment task was due solely to impaired visual imagery. It is important to note, however, that this does not rule out the possibility of visual imagery in sighted subjects. Despite the fact that both sighted and congenitally blind subjects perform equally on the roughness-distance task, it is still possible that these groups do so using very different neural mechanisms.

In sighted subjects, the selective effect of occipital cortex disruption on distance judgment is in line with the view that this cortical area is implicated in the analysis of macrogeometric (i.e., distance) rather than microgeometric (i.e., texture) features (see Sathian et al., 1997; Zangaladze et al., 1999). These results also lend credence to the view that the processing of these attributes may be functionally subdivided (Roland et al., 1998). However, one might expect that disruption of somatosensory cortex would produce a nonspecific effect on both tactile tasks (i.e., impair both roughness and distance judgments), given that this area can be assumed to be the "entry point" of tactile sensory information (Zangaladze et al., 1999). Given the limited depth of penetration of the rTMS pulse, it is possible that only superficial areas within S1 (as opposed to areas 2, 3a, and 3b) were affected and this could account for the selective disruptive effect. Furthermore, distance determinations (especially at greater interdot spacings) may depend on receptors located within deeper subdivisions of S1 and/or long-range projections between somatosensory and visual cortices unaffected by the TMS pulse. An alternative possibility would be to consider that primary sensory areas share similar representa-

tional and processing strategies. Dinse and Schreiner (2002) have argued that sensory processing within early sensory cortical areas (namely touch, vision, and audition) exploit similar computational algorithms. This overlap allows for the unification of object identification and increased object saliency, the hallmark of multisensory integration (Stein and Meredith, 1993). The relative contribution of each cortical area may reflect which modality is most "ideally suited" in providing the information required (Guest and Spence, 2003). Thus, impaired roughness discrimination following disruption of somatosensory cortex would suggest that this area strongly contributes to this type of texture information. Distance discrimination remains intact since the occipital cortex is capable of carrying out fine spatial comparisons, albeit at a lowered overall input drive from somatosensory cortex. Conversely, disrupting occipital cortex impairs fine spatial discrimination (since this area may be more ideally suited for these operations and is being affected directly), but roughness perception is still possible given that processing within somatosensory cortex is still intact. It is also possible that somatosensory and visual cortices represent entry points for rTMS but its effect may be distant from the stimulation site itself. Distance judgments can be carried out within a region (perhaps parietal cortical areas and/or thalamic nuclei) that can be secondarily disrupted by occipital cortex stimulation but not from somatosensory cortex. The fact that patient MC (with her extensive bilateral occipital cortical and subcortical damage) showed greater impairment on the distance task than that induced by occipital rTMS in sighted controls suggests that areas beyond striate cortex are likely implicated in performing this task. Finally, it is difficult to know with certainty which areas were functionally being disrupted through rTMS application. Though stimulation was centered over primary visual cortex, it is likely that peristriate areas were affected as well. Similarly, it is possible that areas within the precentral sulcus were affected during somatosensory cortex stimulation. This latter point becomes more difficult to resolve given that accumulating evidence suggests that rTMS leads to direct effects on the site of stimulation but also affects functionally connected areas (see Paus et al., 1997). Further studies combining TMS with functional imaging are likely to assist in disentangling these important issues.

The implication of occipital cortex in tactile processing may be the result of specialized but complementary inputs that converge onto this region, and it is this overlap that provides the redundancy of cues needed to organize stimuli spatially across different modalities (Johnson and Hsiao, 1992). Areas that typically process one sensory modality can contribute to input obtained from another modality. Despite similar sensory representations and processing strategies, this does not mean that primary cortical areas cannot contribute differently to the overall representation or identification of an object. Viewed in this way, such a framework involving cross-modal sensory processing can confer a behavioral advantage and even be functionally adaptive in conditions when a sensory modality is lost (for example, sight).

Experimental Procedures

Sighted Subjects

Experiments were carried out in accordance with NIH guidelines for human studies and approved by the hospital's Institutional Review Board. All 11 subjects (7 male, aged between 26 and 43) gave informed consent to participate in the study. None of the sighted subjects were familiar with Braille and all had 20/20 best-corrected visual acuity and normal neurologic and physical examinations. Exclusion criteria included any history of neurological disorders (except for patient MC; see below), trauma to hands, calluses at the test finger pad, or any cognitive impairments (including dyslexia). All subjects were strongly right handed (as determined by self-assessment of handedness and administration of the modified Edinburgh handedness inventory questionnaire; Oldfield, 1971).

Congenitally Blind Subjects

In addition to sighted subjects, we assessed tactile performance in five (four male, mean age 19) congenitally blind subjects. All subjects were proficient Braille readers (Grade II Braille) and had best-corrected visual acuity between 20/400 and no light perception. Causes of blindness were trauma, retinopathy of prematurity, congenital glaucoma, and Leber's congenital amaurosis.

Patient MC

We tested tactile performance with an early blind patient secondary to retinopathy of prematurity. This individual, once a highly proficient Braille reader, became alexic for Braille following bilateral ischemic insult to her occipital cortex (see inset of Figure 3). The clinical history has been reported in detail elsewhere (Hamilton et al., 2000).

Stimulus and Task

Stimuli consisted of eight tactile patterns of embossed raised dots (1 mm in diameter, 2 mm in elevation). The dots are arranged in a tetragonal array with constant interdot spacing varying from 1 to 8.2 mm (see Figure 1A). This tactile task and stimuli have been used extensively in neurophysiology and behavioral studies and have been described elsewhere (Connor et al., 1990; Johnson and Hsiao, 1992). Briefly, the task was to judge either the perceived roughness or the perceived interdot distance of the tactile patterns by using a rating scale of 1 to 10 (1 representing most smooth or closest spacing and 10 representing most rough or farthest spacing). Distance and roughness judgments were made separately in alternating blocks of trials. Subjects were instructed to use their own daily experience in judging roughness and distance and to maintain the same strategy of scaling judgments throughout testing. No instruction of the use of visual imagery was made. For testing, the subject's right hand was placed comfortably on an immobilizing plate (palm facing down) with the distal pad of the index finger extended so as to touch the presented patterns. Subjects scanned each surface with their index finger and raised the finger above the surface when the pattern was changed by the experimenter. Two scanning sweeps were allowed per presented pattern, after which subjects were asked to give a response. A restricting wire was used to maintain uniform sweep distance and scanning motions were carefully monitored by the experimenter. Though contact pressure was not measured, previous studies have suggested that tactile resolution is relatively independent of contact force and the rate of application (van Boven and Johnson, 1994; Sathian and Zangaladze, 1996). Responses represent the mean of three total randomized presentations for each task.

TMS

TMS was delivered using a MagStim stimulator (MagStim, Whitland, UK) and a 70 mm figure of eight coil to the somatosensory and the occipital cortex. For control purposes (on a separate day), performance was assessed following stimulation to the vertex (Cz). Left sensorimotor cortex stimulation was carried out by placing the TMS coil tangentially on the scalp 1.5 cm posterior to the optimal position for induction of motor-evoked potentials in the contralateral first dorsal interosseus (FDI). Visual cortex stimulation was determined by placing the TMS coil 2 cm above the inion and centered on the midline. Correct site of stimulation was insured a posteriori

by comparing scalp position coregistered with the subject's own anatomical MRI using a frameless stereotaxic-based system (Brainsight; Montreal, Canada) (see Figure 1C). TMS intensity was set at 110% of the subject's motor threshold (defined following current safety guidelines; Wassermann, 1998). Stimulation intensities ranged between 45% and 82% of maximum stimulator output. TMS was always applied using a 10 min train of 1 Hz repetitive stimulation. During rTMS, no motor-evoked potentials and hand movements or phosphenes were induced by somatosensory and occipital stimulation, respectively.

Experimental Protocol

After a trial to familiarize subjects with the eight pattern stimuli (while blindfolded and not requiring a response), subjects were instructed on the task and given earplugs, and then they began the experiment (see Figure 1B for experimental design). At no time were the sighted subjects allowed to visually examine the tactile stimuli. The offline design consisted of one block prior to the TMS sessions for assessing baseline performance followed by two blocks post-TMS stimulation. Previous studies have suggested that repetitive TMS at low frequency (1 Hz) temporarily reduces excitability of the stimulated cortex that outlasts the period of stimulation and is accompanied by behavioral changes within a time window between 5 and 20 min (Chen et al., 1997; Boroojerdi et al., 2000; Knecht et al., 2003). To maximize the potential behavioral effect, we designed the testing phase of the experiment to be completed within a 5 min window after the end of the rTMS session. After completion of the first post-TMS session, a rest ("washout") period of 30 min was observed before the next block in order to avoid any crossover effects between stimulation sites. Site of stimulation (somatosensory and occipital) and task order were randomized and counter-balanced across all subjects. The experiment lasted approximately 1 hr.

Statistical Analysis

For TMS effects in sighted subjects, data were subjected to 3×8 analyses of variance (ANOVA, repeated measure) with TMS (baseline versus postsomatosensory versus postoccipital/PRE versus S1 versus V1) and tactile pattern (1–8) as within-subject factors to evaluate the effect of rTMS on roughness and distance judgment, respectively. Scheffé test were applied for post hoc comparisons. For comparisons between sighted and congenitally blind subjects, baseline values were compared for roughness and distance judgment separately using a 2×8 ANOVA [(sighted versus blind; between group factor) \times (tactile pattern 1–8; within subject factor)].

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References

- Amedi, A., Jacobson, G., Hendler, T., Malach, R., and Zohary, E. (2002). Convergence of visual and tactile shape processing in the human lateral occipital complex. *Cereb. Cortex* 11, 1202–1212.
- Buchel, C., Price, C., Frackowiak, R.S., and Friston, K. (1998). Different activation patterns in the visual cortex of late and congenitally blind subjects. *Brain* 121, 409–419.
- Burton, H., Snyder, A.Z., Conturo, T.E., Akbudak, E., Ollinger, J.M., and Raichle, M.E. (2002). Adaptive changes in early and late blind: a fMRI study of Braille reading. *J. Neurophysiol.* 87, 589–607.
- Boroojerdi, B., Prager, A., Muellbacher, W., and Cohen, L.G. (2000). Reduction of human visual cortex excitability using 1-Hz transcranial magnetic stimulation. *Neurology* 54, 1529–1531.

- Borojerdi, B., Meister, I.G., Foltys, H., Sparing, R., Cohen, L.G., and Topper, R. (2002). Visual and motor cortex excitability: a transcranial magnetic stimulation study. *Clin. Neurophysiol.* 113, 1501–1504.
- Chen, R., Classen, J., Gerloff, C., Celnik, P., Wassermann, E.M., Hallett, M., and Cohen, L.G. (1997). Depression of motor cortex excitability by low-frequency transcranial magnetic stimulation. *Neurology* 48, 1398–1403.
- Cohen, L.G., Celnik, P., Pascual-Leone, A., Corwell, B., Falz, L., Dambrosia, J., Honda, M., Sadato, N., Gerloff, C., Catala, M.D., and Hallett, M. (1997). Functional relevance of cross-modal plasticity in blind humans. *Nature* 389, 180–183.
- Connor, C.E., Hsiao, S.S., Phillips, J.R., and Johnson, K.O. (1990). Tactile roughness: neural codes that account for psychophysical magnitude estimates. *J. Neurosci.* 12, 3823–3836.
- Deibert, E., Kraut, M., Kremen, S., and Hart, J., Jr. (1999). Neural pathways in tactile object recognition. *Neurology* 52, 1413–1417.
- Dinse, H.R., and Schreiner, C.E. (2002). Do primary sensory areas play analogue roles in different sensory modalities? In *Cortical Areas: Unity and Diversity*, A. Schüz and R. Miller, eds. (London: Taylor and Francis Group), pp. 273–310.
- Guest, S., and Spence, C. (2003). Tactile dominance in speeded discrimination of textures. *Exp. Brain Res.* 150, 201–207.
- Hamilton, R., Keenan, J.P., Catala, M., and Pascual-Leone, A. (2000). Alexia for Braille following bilateral occipital stroke in an early blind woman. *Neuroreport* 11, 237–240.
- Johnson, K.O., and Hsiao, S.S. (1992). Neural mechanisms of tactual form and texture perception. *Annu. Rev. Neurosci.* 15, 227–250.
- Knecht, S., Ellger, T., Breitenstein, C., Bernd Ringelstein, E., and Henningsen, H. (2003). Changing cortical excitability with low-frequency transcranial magnetic stimulation can induce sustained disruption of tactile perception. *Biol. Psychiatry* 53, 175–179.
- Lederman, S.J. (1982). Perception of texture by touch. In *Tactual Perception*, W. Schiff and E. Foulke, eds. (Cambridge, UK: Cambridge University Press), pp. 130–167.
- Macaluso, E., Frith, C.D., and Driver, J. (2000). Modulation of human visual cortex by crossmodal spatial attention. *Science* 289, 1206–1208.
- Meftah, el-M., Shenasa, J., and Chapman, C.E. (2002). Effects of a cross-modal manipulation of attention on somatosensory cortical neuronal responses to tactile stimuli in the monkey. *J. Neurophysiol.* 88, 3133–3149.
- Oldfield, R.C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9, 97–113.
- Pascual-Leone, A., Walsh, V., and Rothwell, J. (2000). Transcranial magnetic stimulation in cognitive neuroscience—virtual lesion, chronometry, and functional connectivity. *Curr. Opin. Neurobiol.* 2, 232–237.
- Paus, T., Jech, R., Thompson, C.J., Comeau, R., Peters, T., and Evans, A.C. (1997). Transcranial magnetic stimulation during positron emission tomography: a new method for studying connectivity of the human cerebral cortex. *J. Neurosci.* 17, 3178–3184.
- Robertson, E.M., Theoret, H., and Pascual-Leone, A. (2003). Studies in cognition: the problems solved and created by transcranial magnetic stimulation. *J. Cogn. Neurosci.* 15, 948–960.
- Roder, B., Stock, O., Bien, S., Neville, H., and Rosler, F. (2002). Speech processing activates visual cortex in congenitally blind humans. *Eur. J. Neurosci.* 16, 930–936.
- Roland, P.E., O’Sullivan, B., and Kawashima, R. (1998). Shape and roughness activate different somatosensory areas in the human brain. *Proc. Natl. Acad. Sci. USA* 95, 3295–3300.
- Sadato, N., Pascual-Leone, A., Grafman, J., Ibanez, V., Deiber, M.P., Dold, G., and Hallett, M. (1996). Activation of the primary visual cortex by Braille reading in blind subjects. *Nature* 380, 526–528.
- Sadato, N., Okada, T., Honda, M., and Yonekura, Y. (2002). Critical period for cross-modal plasticity in blind humans: a functional MRI study. *Neuroimage* 2, 389–400.
- Sathian, K., and Zangaladze, A. (1996). Tactile spatial acuity at the human fingertip and lip: bilateral symmetry and interdigit variability. *Neurology* 46, 1464–1466.
- Sathian, K., Zangaladze, A., Hoffman, J.M., and Grafton, S.T. (1997). Feeling with the mind’s eye. *Neuroreport* 8, 3877–3881.
- Stein, B.E., and Meredith, M.A. (1993). *The Merging of the Senses* (Cambridge, MA: The MIT Press).
- Van Boven, R.W., and Johnson, K.O. (1994). The limit of tactile spatial resolution in humans: grating orientation discrimination at the lip, tongue, and finger. *Neurology* 44, 2361–2366.
- Wassermann, E.M. (1998). Risk and safety of repetitive transcranial magnetic stimulation: report and suggested guidelines from the International Workshop on the Safety of Repetitive Transcranial Magnetic Stimulation, June 5–7, 1996. *Electroencephalogr. Clin. Neurophysiol.* 108, 1–16.
- Zangaladze, A., Epstein, C.M., Grafton, S.T., and Sathian, K. (1999). Involvement of visual cortex in tactile discrimination of orientation. *Nature* 401, 587–590.