

Combined Activation and Deactivation of Visual Cortex During Tactile Sensory Processing

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¹Perceptual Neuroimaging Laboratory, Department of Psychology and Program in Neuroscience, Boston University, Boston; ²Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Charlestown; and ³Center for Non-Invasive Brain Stimulation, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts

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Merabet LB, Swisher JD, McMains SA, Halko MA, Amedi A, Pascual-Leone A, Somers DC. Combined activation and deactivation of visual cortex during tactile sensory processing. *J Neurophysiol* 97: 1633–1641, 2007. First published November 26, 2006; doi:10.1152/jn.00806.2006. The involvement of occipital cortex in sensory processing is not restricted solely to the visual modality. Tactile processing has been shown to modulate higher-order visual and multisensory integration areas in sighted as well as visually deprived subjects; however, the extent of involvement of early visual cortical areas remains unclear. To investigate this issue, we employed functional magnetic resonance imaging in normally sighted, briefly blindfolded subjects with well-defined visuotopic borders as they tactually explored and rated raised-dot patterns. Tactile task performance resulted in significant activation in primary visual cortex (V1) and deactivation of extrastriate cortical regions V2, V3, V3A, and hV4 with greater deactivation in dorsal subregions and higher visual areas. These results suggest that tactile processing affects occipital cortex via two distinct pathways: a suppressive top-down pathway descending through the visual cortical hierarchy and an excitatory pathway arising from outside the visual cortical hierarchy that drives area V1 directly.

INTRODUCTION

Increasing evidence suggests that occipital cortex, in addition to its visual functions, is implicated in processing information from other sensory modalities (Sathian 2005; Schroeder and Foxe 2005; Sur and Leamey 2001). For example, after prolonged visual deprivation, visual cortex is recruited in a compensatory manner to process both tactile and auditory information (Burton et al. 2002; Gougoux et al. 2004; Kujala et al. 1995; Roder et al. 2002; Sadato et al. 1996). However, the extent of early visual cortex's involvement in cross-modal processing in sighted subjects remains contentious, especially the possible involvement of primary visual area V1 (Amedi et al. 2001, 2002; Burton et al. 2004, 2006; Macaluso et al. 2000; Merabet et al. 2004; Reed et al. 2004; Sathian et al. 1997; Van Boven et al. 2005; Weisser et al. 2005; Zangaladze et al. 1999; Zhang et al. 2005). This issue is further complicated by the wide variability between individuals in the size and location of retinotopically organized visual areas (Dougherty et al. 2003), which makes the localization of group-level activations problematic.

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The cerebral networks and neuroplastic mechanisms underlying the cross-modal activation of sensory cortex remain unclear (see Bavelier and Neville 2002 for review). It has been suggested that top-down signals originating within multimodal associative cortical areas may selectively recruit appropriate primary sensory areas (Macaluso et al. 2000). Alternatively, cross-modal activity may be mediated by plastic changes in subcortical pathways (Sur and Leamey 2001). However, there is little existing evidence to support this as a mechanism in the intact adult brain. Another possibility is the involvement of direct, long-range cortico-cortical pathways connecting primary sensory cortex with other sensory or multimodal cortices. This latter proposition has received support from both anatomical and connectivity studies demonstrating the existence of direct connections to V1 from both unimodal cortex and conventional multimodal areas (Cappe and Barone 2005; Clavagnier et al. 2004; Falchier et al. 2002; Negyessy et al. 2006; Rockland and Ojima 2003).

These models make different predictions about how cross-modal inputs may influence cortical activity across the sensory processing hierarchy. A hierarchical feedback model would suggest that the greatest cross-modal influences should be seen in higher sensory areas, analogous to the patterns of activity seen in studies of visual attention (Kastner et al. 1998; Somers et al. 1999), imagery (Kosslyn and Thompson 2003), and other classically “top-down” phenomena. Conversely, either a subcortical or a direct connectivity model allows for the possibility of “bottom-up” activation of primary sensory areas (Foxe and Schroeder 2005), without the necessary involvement of higher-order cortex. Importantly, these possibilities are not mutually exclusive: multiple pathways could carry distinct information (Schroeder and Foxe 2005) or act cooperatively or competitively to facilitate multisensory integration (Grossberg and Kuperstein 1989; Pouget et al. 2002).

In this study, we acquired retinotopic maps to precisely identify visual cortical areas within individual normally sighted subjects. These subjects then performed a tactile discrimination task while blindfolded. We find that tactile processing activates area V1, while higher extrastriate areas show a pattern of increasing blood-oxygen-level-dependent (BOLD) signal suppression as one ascends the visual cortical hierarchy. This pattern of activity is consistent with the combined effect of

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direct activation of primary visual cortex and top-down suppression of extrastriate cortex.

METHODS

Subjects

Experiments were carried out in accordance with MR safety guidelines and National Institutes of Health standards for human studies and were approved by the Institutional Review Boards of Massachusetts General Hospital and Boston University. Twelve normally sighted subjects (aged between 20 and 32 yr, 11 right-handed) participated in the study.

Tactile stimuli and task

Stimuli consisted of seven tactile patterns of raised embossed dots. The dots were 1 mm in diameter, 2 mm in elevation, and arranged in tetragonal arrays the inter-dot spacing of which varied from 1 to 7 mm (Fig. 1A). Subjects performed two different tactile tasks using these stimuli, which have been described in detail previously (Connor et al. 1990; Merabet et al. 2004). Briefly, subjects judged either the perceived roughness or the inter-dot spacing of the tactile patterns. Task responses used a 1–4 rating scale with “1” representing most smooth, or closest spacing, and “4” representing roughest, or farthest spacing. During scanning, the subject’s right hand was placed comfortably on an immobilizing plate, palm down, with the distal pad of the index finger extended so as to touch the presented patterns. Between trials, subjects raised their finger above the surface as the pattern was changed by the experimenter. Two scanning sweeps of the finger were allowed per presented pattern, after which subjects responded using a button box placed under their left hand. Two control conditions were used. In the “active” control condition, subjects were presented with a smooth surface (no dots), sweeping in the same fashion as with the tactile patterns while responding with random key presses. In the “passive” control condition, subjects rested without moving either hand. The four conditions occurred in 30-s blocks preceded by an auditory task cue. Subjects were blindfolded on being placed in the magnet, with the total time blindfolded averaging ~90 min. At no time prior to the scanning session were the subjects allowed to see the tactile stimuli.

Image acquisition

MR images were acquired using a 3T Siemens Allegra scanner (Erlangen, Germany) located at the Martinos Center for Biomedical

Imaging at Massachusetts General Hospital. Functional data were acquired with a custom-made surface coil (Nova Medical, Wilmington, MA) placed at the occipital pole and using a T2*-weighted echo planar imaging sequence (TR = 2.0 s, TE = 30 ms, $2.8 \times 2.8 \times 3.0$ mm voxels, 0.3-mm interslice gap, 30 slices oriented perpendicular to the calcarine sulcus). The slice prescription extended anteriorly roughly to the central sulcus in most subjects.

Retinotopic mapping and region of interest (ROI) definition

Standard wedge (polar angle) and ring (eccentricity) checkerboard stimuli were presented during the retinotopic mapping sessions and were subsequently combined and averaged using previously described techniques (DeYoe et al. 1996; Engel et al. 1994, 1997; Sereno et al. 1995). Areas V1, V2, V3, V3A (Tootell et al. 1997), and hV4 (Brewer et al. 2005; Wade et al. 2002) were identified on the basis of these maps in all subjects. As the representations of the upper and lower visual field are not contiguous in areas V2 and V3, separate ROIs were defined for each quadrant in these areas and in area V1. In areas V3A and hV4, separate ROIs were defined for each cortical hemisphere. These regions represent the visual field from an eccentricity of $\sim 2^\circ$ out to 12° visual angle. The representation of polar angle converges in a mathematical singularity at the fovea, and thus areal boundaries near the fovea are ill-defined. For this reason, the foveal representation was excluded from the defined ROIs. An alternative set of V1 ROIs that included the fovea were defined by interpolating areal boundaries across the foveal singularity, but this had a negligible effect on the average signal and did not alter any of the statistical conclusions. Therefore we report the results only for the more conservative ROI definitions.

Analysis

Data analysis used FreeSurfer software (Dale et al. 1999; Fischl et al. 1999a) and FS-FAST (FreeSurfer functional analysis stream; CorTechs, La Jolla, CA). Two runs from one subject exhibited substantial (>3 mm) motion artifacts and so were excluded from further analysis. After motion correction (Cox and Hyde 1997) and spatial smoothing (Gaussian kernel, 5.0 mm FWHM), voxel time courses for each individual subject were fit by a general linear model (GLM). Each experimental condition, plus the transient auditory cue that began each block, was modeled by a boxcar regressor matching the condition time course. These boxcar regressors were then smoothed by a canonical hemodynamic response function (Boynton et al. 1996). Individual subject maps for each contrast of interest (described in RESULTS) were generated by projecting the volume of significance values resulting from the GLM onto the reconstructed cortical surface mesh (Dale et al. 1999) for each hemisphere in each subject. These cortical meshes were then computationally inflated and flattened for display (Fischl et al. 1999a).

For population random-effects analysis, the volumes of regressor weights resulting from the individual subject GLMs were first projected onto the reconstructed cortical surfaces as in the preceding text. These individual cortical surfaces were then deformed into a common spherical coordinate system (Fischl et al. 1999a,b). Group analysis used a summary statistic approach at the second level, with individual subject regressor weights combined at each vertex by a *t*-test for each contrast of interest. This generates a population *t* statistic map ($df = 11$) in spherical coordinates for each contrast. The significance maps derived from these statistics were then projected back onto the inflated cortical surface of a single representative subject for display.

To correct for multiple comparisons, the AFNI program AlphaSim (BD Ward, <http://afni.nimh.nih.gov/>) was used to establish cluster-wise thresholds for the population maps based on Monte Carlo simulation of a smoothed null hypothesis data set (Forman et al. 1995). The Monte Carlo simulation generated random volumes of normally distributed values, which were then smoothed by a 5-mm

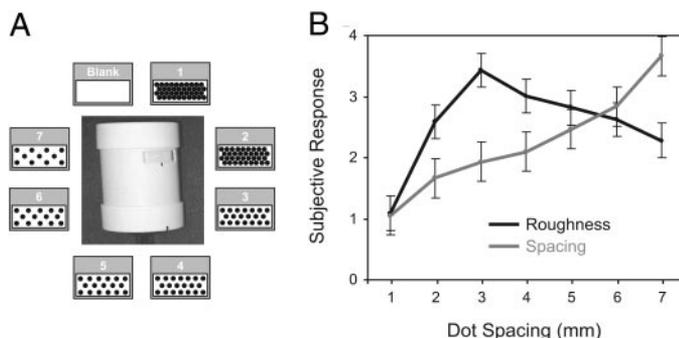


FIG. 1. Tactile stimuli and behavioral task performance. *A*: seven raised dot patterns of varying inter-dot spacing (including 1 blank pattern) were presented with a rotating drum controlled by the experimenter (see inset). Using their index finger, subjects were instructed to judge either the roughness or spacing between dots of the tactile patterns. *B*: mean performance for the tactile tasks. Subject responses for roughness (black) and spacing (gray) judgments are plotted against actual dot spacing. See text for complete description of behavioral task.

FWHM kernel. The topmost 5% of simulated voxels (for a P value of 0.05) were considered to be active and assigned a value of 1 with the rest set to 0. These volumes were then masked to include only those voxels that intersected the reconstructed cortical surface, and the maximum cluster size of adjacent active simulated voxels was found. Over 1,000 iterations of this process, we found that under this simulated null hypothesis, a joint threshold of 340 mm² cluster surface area and $P < 0.05$ pointwise significance was sufficient to establish a clusterwise significance level of $P < 0.05$. All reported activations outside retinotopic cortex are significant at this clusterwise level.

In the ROI-based analysis, the time series data for all voxels within an individual subject's ROI were first averaged together and then fit by the same GLM as used for the voxelwise individual subjects analysis described in the preceding text. The resulting parameter estimates, one per experimental condition per ROI per subject, were then normalized to percent signal change units and entered into a within-subjects ANOVA for second level group analysis, described in RESULTS.

RESULTS

Psychophysical performance on the tactile discriminations was similar to previous reports (Connor et al. 1990; Merabet et

al. 2004). Intermediate dot spacings were perceived as the roughest, whereas closely and widely spaced dot patterns felt comparatively smoother. In contrast, subjective spacing judgments increased linearly with actual dot spacing (see Fig. 1B).

Cortical surface-based analysis

We investigated task-general and -specific tactile activation. Task-general activation was assessed by the contrast of the averaged spacing and roughness tasks versus the active control condition. Task-specific activation was assessed by the contrast of the spacing and roughness tasks. Random-effects analysis of the population data shows significant tactile task-general activation within the calcarine sulcus, coupled with extrastriate suppression (Fig. 2, A and B). This pattern of activity within retinotopically organized visual cortex is the main focus of this report and will be discussed in detail in the following text.

The task-general contrast also shows significant bilateral activation along the intraparietal sulcus (IPS) (Fig. 2B; Table 1). Additional activation was found bilaterally within the inferior temporal gyrus, immediately anterior and ventral to the

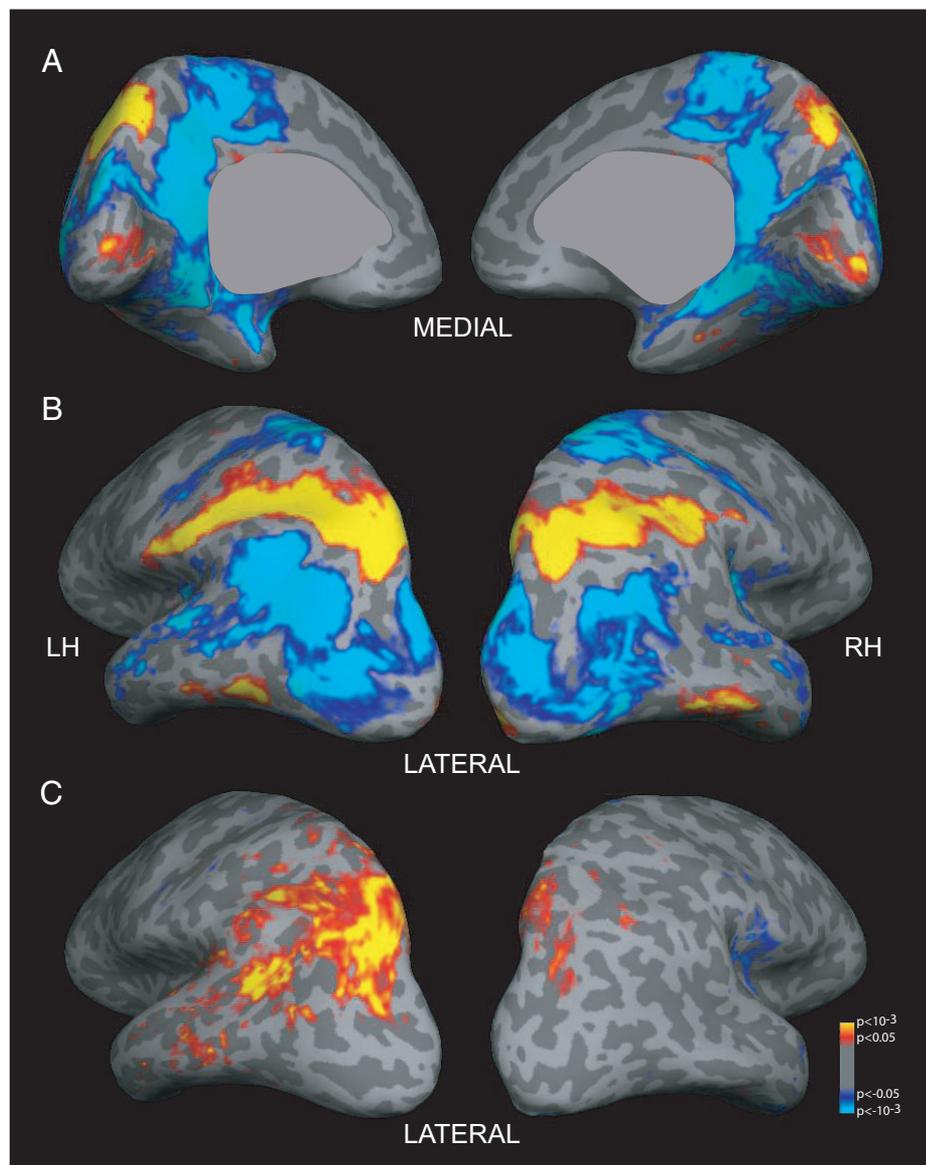


FIG. 2. Group activation maps on inflated cortex. Random-effects population maps are shown projected onto the inflated cortical hemispheres of a single subject. The task-general contrast (average spacing and roughness tasks vs. active control) is shown in A (medial view) and B (lateral view), while the task-specific contrast (spacing vs. roughness) is displayed in C. There was no significant task-specific activation on the medial surface. All activity is shown thresholded at a $P < 0.05$ voxelwise level (see tables for clusterwise significances). Task-general activation extends along the intraparietal sulcus (IPS) bilaterally, with separate regions of activity in ventral occipital/inferior temporal cortex. Activity is also seen along the calcarine sulcus. Wide regions of cortex exhibit task-general deactivation, including the precuneus, extrastriate visual cortex, the posterior part of the superior temporal sulcus (STS), and medial regions of the central and postcentral sulci. Greater activation for the spacing task is seen along the left IPS extending into the STS, with weaker activation of the corresponding regions of the right hemisphere (ipsilateral to the stimulated hand). Regions anterior to the central sulcus were not included in the slice prescription, and so the lack of visible activation in these regions should not be interpreted as reflecting a true absence of activity. LH, left hemisphere; RH, right hemisphere.

TABLE 1. *Task > active control*

Brain Region	Laterality	x	y	z	Cluster Size, mm ²
IPS	LH	-22.0	-59.8	43.1	5203.2
IPS	RH	33.5	-61.0	44.6	4200.9
Inferior temporal	RH	52.1	-51.0	-9.0	670.6
Inferior temporal	LH	-47.6	-58.0	-1.8	361.5
V1	LH	-1.0	-101.3	0.9	365.6

Right V1 activity in the population map falls into two separate clusters and so does not exceed the cluster size threshold despite being comparable in total size to left V1 activation. Only activity significant at a $P < 0.05$ clusterwise level is shown. IPS, intraparietal sulcus; LH and RH, left and right hemisphere.

MT+ complex. Wide regions of bilateral task-general suppression (active control > averaged tactile tasks) are also evident, including the posterior end of the superior temporal sulcus (STS) and the precuneus, extending into the posterior cingulate gyrus and parieto-occipital sulcus (Table 2).

The task-specific contrast revealed significantly greater activation during the spacing task in the left IPS extending into the STS (Fig. 2C, Table 3). Equivalent regions of the right hemisphere, ipsilateral to the stimulated finger, were only weakly activated in this contrast and did not reach significance on a clusterwise level. No areas were observed to be significantly more active during roughness judgments.

Comparison of the two control conditions revealed greater activation during the active control periods (which include motor activity and task-irrelevant somatosensory stimulation) than during rest within the central and postcentral sulcus bilaterally (Table 4). Reduced activity during the active control relative to rest was found within many of the same regions that exhibited task-general deactivation (Table 5). Regions anterior to the central sulcus were not included in our slice prescription and so could not be characterized in this study.

Activation patterns in early visual cortex

Visual cortical areas V1, V2, V3, V3A, and hV4 were identified bilaterally in each subject using retinotopic mapping

TABLE 2. *Active control > task*

Brain Region	Laterality	x	y	z	Cluster Size, mm ²
Precuneus/postcentral/POS	LH	-13.9	-39.2	34.6	3620.32
STS	LH	-38.7	-76.3	27.5	2477.8
Postcentral (medial)	RH	18.8	-39.2	57.1	2145.7
Precuneus/parietal-occipital sulcus	RH	26.6	-55.2	22.3	1204.9
Medial temporal	RH	31.5	-27.4	-6.3	801.1
STS	RH	41.7	-57.2	27.3	718.78
Medial temporal	LH	-26.2	-38.5	-4.5	717.2
Extrastriate/V7	LH	-18.2	-87.9	30.0	595.9
Postcentral (dorsal)	LH	-16.0	-29.0	73.2	573.4
Extrastriate/V3A	RH	27.0	-87.3	15.4	567.3
Ventral extrastriate	RH	34.7	-72.8	-11.2	435.6
Extrastriate/V7	RH	24.5	-85.5	33.1	381.7

These regions of deactivation appear as one significant contiguous cluster at the lower ($P < 0.05$) voxelwise threshold used in other contrasts. To better illustrate the separate foci of deactivation, these clusters are indicated at a $P < 0.01$ voxelwise threshold. As a result, cluster sizes in this contrast are not comparable to those in other tables. STS, superior temporal sulcus.

TABLE 3. *Spacing > roughness*

Brain Region	Laterality	x	y	z	Cluster Size, mm ²
IPS	LH	-13.8	-77.6	38.5	6209.9
Postcentral (medial)	LH	-17.8	-44.1	64.1	428.9

There were no significant clusters in the right hemisphere. Additionally, no regions were significantly more active during roughness judgments than spacing judgments.

techniques (see METHODS). Area V1 was bilaterally activated by the tactile tasks (combined tactile > active control) in 9 of 12 subjects. Statistical maps for single subjects show that this activation is largely restricted to area V1, with little or no activation observed in V2 (Fig. 3). No clear pattern of eccentricity-specific influences in V1 was observed. Specifically, four subjects showed robust activation relatively uniformly throughout V1; two subjects had activity concentrated at the foveal representation; and three subjects had strong parafoveal activation that largely spared the fovea.

Extrastriate cortical areas were strongly deactivated in this task-general contrast with the greatest BOLD suppression in areas V3 and V3A. This suppression was readily apparent in 10 of 12 individual subjects. Additionally, the MT+ complex was identified in six subjects using a low-contrast motion stimulus (LCMS) (Tootell et al. 1995) (the remaining 6 subjects did not view the LCMS due to time constraints). In all these subjects, MT+ was found to be significantly deactivated during tactile stimulation (Fig. 3).

ROIs for areas V1, V2, V3, V3A, and hV4 were defined within each subject for each visual field quadrant representation (left/right, dorsal/ventral) based on the retinotopic mapping data (see METHODS). Time courses extracted from these ROIs confirm the pattern of task-general tactile activation of V1 and deactivation of higher areas indicated by the statistical maps (Fig. 3). The average percent signal change data shows increasing task-related BOLD suppression as one ascends through the visual hierarchy from area V2 through V3 and V3A (Fig. 4A). To investigate the significance of this trend, as well as the possibility of effects based on laterality or differences between dorsal and ventral quadrant representations (Prather et al. 2004; Reed et al. 2005; Van Boven et al. 2005), the percent signal change data within areas V1–V3 were entered into a within-subjects ANOVA. Factors included in the ANOVA were area (V1, V2, V3), hemi (left, right), D/V (dorsal or ventral subregions), and task (spacing, roughness, active control) together with all interaction terms. The passive control condition defined the zero signal change baseline and so did not enter explicitly into the analysis. The analysis showed substantial main effects of area [$F(2,22) = 19.4$, $P < 0.001$] and D/V [$F(1,11) = 25.0$, $P < 0.001$] as well as significant task:area [$F(4,44) = 26.8$, $P < 0.001$] and task:D/V [$F(2,22) = 12.8$, $P < 0.001$] interactions and a marginally significant area:hemi interaction [$F(2,22) = 3.5$, $P < 0.05$].

TABLE 4. *Active > passive control*

Brain Region	Laterality	x	y	z	Cluster Size, mm ²
Central/postcentral sulcus	LH	-36.8	-24.1	48.6	4722.8
Central/postcentral sulcus	RH	14.0	-68.1	61.8	2137.6
Postcentral sulcus (lateral)	LH	-53.3	-22.3	16.6	641.6

TABLE 5. *Passive > active control*

Brain Region	Laterality	x	y	z	Cluster Size, mm ²
Precuneus	LH	-15.3	-40.3	35.1	4722.8
Parietal-occipital sulcus	LH	-8.5	-62.4	25.1	1353.9
STS/IPS	LH	-36.5	-79.0	28.8	1310.8
Precuneus	RH	18.9	-42.8	37.6	854.7
Parietal-occipital sulcus	RH	8.2	-61.0	28.5	769.0
STS/IPS	RH	42.4	-79.4	23.5	541.6

The task:area interaction is of greatest interest and confirms the significance of the areal differences shown in Fig. 4A.

The interactions with task appeared to reflect primarily differences between the active control condition and the two tactile judgments and not differential activity between the spacing and roughness judgments themselves. This interpretation is supported by further analysis. We entered the data from the two tactile tasks only into a second ANOVA, omitting the active control data. As expected, this restricted analysis showed significant main effects of area [$F(2,22) = 25.4, P <$

0.001], reflecting increasing task-general suppression in higher visual areas and D/V [$F(1,11) = 45.0, P < 0.001$] but no effect of task, showing that the spacing and roughness judgments did not produce significantly different activity in early visual cortex. An ANOVA including only the active control data revealed no significant effects, indicating that motor activity alone did not differentially modulate any of these cortical regions. Furthermore, active control activity did not differ appreciably from the passive baseline [paired t -test, $t(11) = -1.1, P > 0.1$]. These analyses demonstrate that the task:area interaction in the main ANOVA reflects task-general tactile processing, rather than task-specific effects.

The unexpectedly large D/V effect reflected substantially lower activation (equivalently, increased suppression) in the dorsal quadrants relative to the ventral quadrants throughout these areas (Fig. 4A). The increased suppression seen in dorsal subregions could potentially represent a retinotopically specific modulation of the lower visual field (LVF) representation rather than an effect based on dorsal versus ventral stream anatomy. However, comparison of areas V3A and hV4 argues

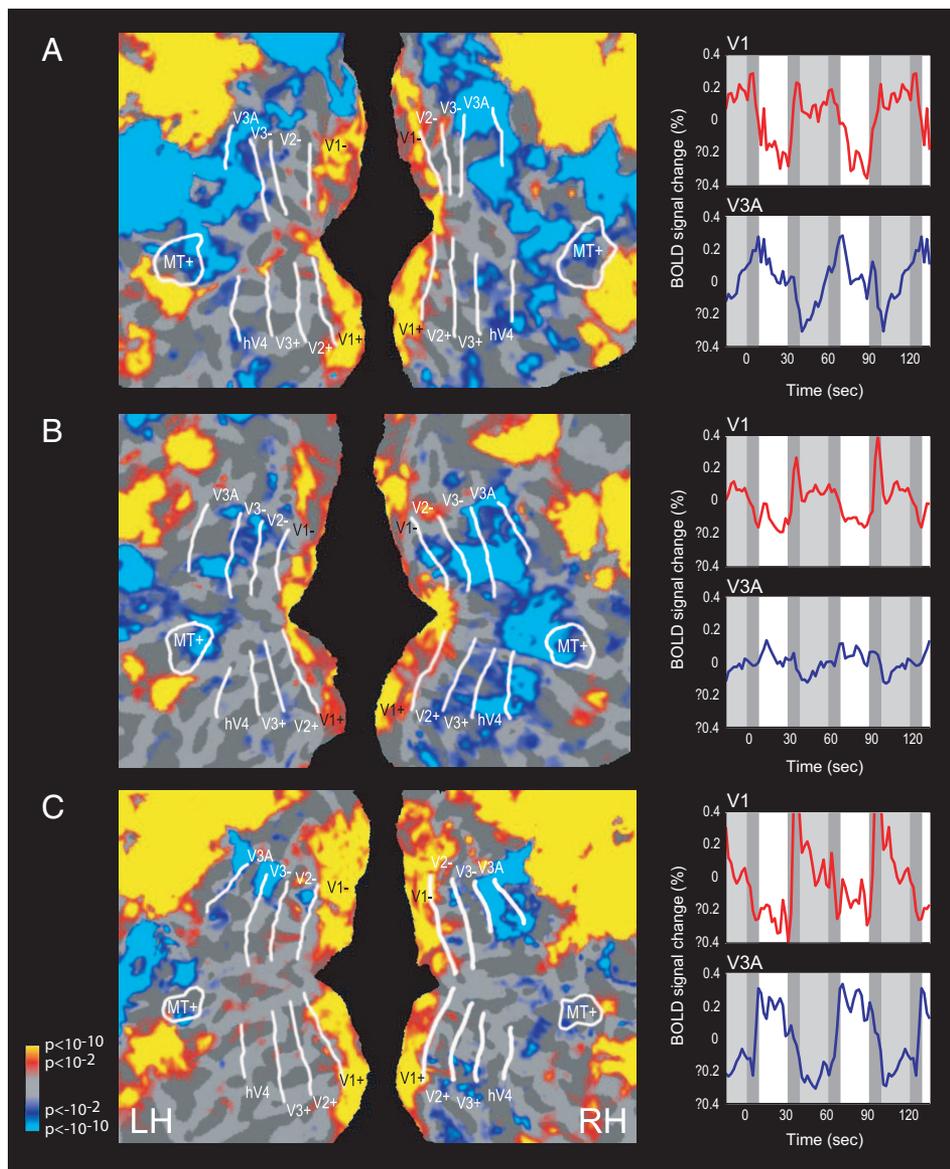


FIG. 3. Individual subject activations in occipital cortex. Individual tactile task-general (averaged spacing and roughness tasks vs. active control) activity is shown bilaterally on the flattened occipital cortical surfaces of 3 subjects. Within early visual cortex, tactile task activation is found within V1 bilaterally. Task-related suppression is seen in extrastriate areas. Strong activation outside retinotopic cortex is centered along the intraparietal sulcus (IPS), with a separate focus in inferior temporal/ventral occipital cortex. Time courses for the V1 (top) and V3A (bottom) regions of interest (ROIs) exhibit an anti-phase relationship. Lightly shaded regions represent blocks of tactile stimulation (spacing or roughness tasks), whereas unshaded areas represent blocks of the control conditions (active or passive). The dark shaded bands indicate “cue” condition time points, which were included in the model as regressors of no interest. Plus, upper visual field; minus, lower visual field.

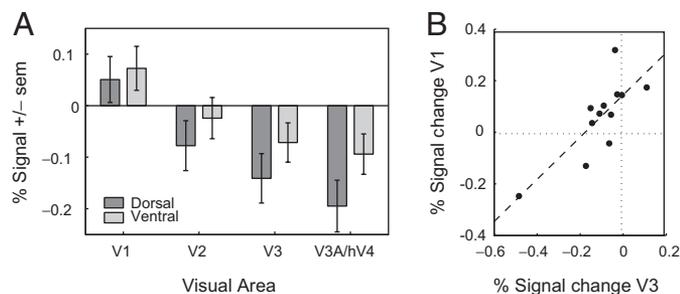


FIG. 4. Group data across retinotopic areas. *A*: average task-general percent signal change is shown for the tactile tasks contrasted with the active control across retinotopically defined areas. Tactile activation is seen in V1, with progressively stronger blood-level-oxygen-dependent signal suppression in V2, V3, and V3A. Across all areas, dorsal subregions are significantly less active (more suppressed) during tactile processing than are ventral subregions. Error bars represent SE. *B*: mean signal change during tactile processing within V1 and V3 for all 12 individual subjects. The dashed line shows the best least-squares fit. Increased V1 activation is associated with reduced suppression of V3, suggesting an underlying functional connectivity between these regions (see text). Eight of 12 subjects show simultaneous activation of V1 and suppression of V3 with no subjects showing the opposite pattern.

against this interpretation; although both areas contain contiguous representations of upper and lower visual quadrants, the dorsally located V3A shows far greater deactivation. Further subdividing these areas into quadrant ROIs reveals no significant differences in activation between the lower and upper visual field representations within these two areas, suggesting that the greater dorsal suppression reflects anatomical rather than retinotopic position.

There are two parsimonious hypotheses that can explain the observed pattern of occipital lobe activity. The *single-source* or *disinhibition hypothesis* states that occipital lobe receives only a single, deactivating source of tactile input that most strongly affects higher visual areas. In this model, the activation observed in V1 reflects disinhibition: if extrastriate cortex normally suppresses striate cortex, then deactivation of extrastriate cortex would release striate cortex from top-down inhibition, resulting in increased V1 activity overall. This hypothesis implies that greater deactivation of extrastriate cortex would result in greater activation within V1. Alternatively, the *dual-source hypothesis* states that occipital lobe receives two distinct sources of tactile input, a deactivating source that dominates extrastriate activity (as in the single-source hypothesis) and an additional activating source that most strongly influences striate cortex. The strong reciprocal connections between striate and extrastriate cortex suggest that these two inputs may compete for influence throughout the early visual areas. Thus the dual-source hypothesis predicts a positive correlation between extrastriate and striate activity. To test these hypotheses, we calculated the correlation between task-related signal change in areas V1 and V3 across individual subjects. Significant negative correlation would imply that greater V3 suppression is associated with greater V1 activation, in support of the disinhibition hypothesis. However, we instead find a significant positive correlation (Pearson's $r = 0.78$, $P < 0.001$), demonstrating that greater V3 suppression is associated with reduced V1 activation, and further suggesting that these areas are modulated by the same competitive network (Fig. 4*B*). Similar results are obtained comparing V1 and V2, and V1 and V3A/hV4. The positive correlation is consistent with the dual-

source hypothesis while failing to support the disinhibition hypothesis.

Prior studies have shown that short-term blindfolding of sighted subjects leads to rapid increases in both the excitability of visual cortex (after 45 min) (Boroojerdi et al. 2000) and tactile acuity (after 90 min) (Facchini and Aglioti 2003). The tactile drive to area V1 in the present study may reflect this rapid cortical plasticity. This 90-min period of visual deprivation might unmask or facilitate preexisting tactile inputs to visual cortex (Pascual-Leone et al. 2005). Although the present study was not explicitly designed to test this rapid plasticity hypothesis, we were able to partially address this question by comparing data from the first half of each subject's session with the data from the second half of the session. The rapid plasticity hypothesis predicts that the amplitude of task-general V1 activation should be greater in the second half of the session for each subject. The V1 data support this hypothesis, showing a marginally significant increase in average tactile task amplitude (vs. passive control) across the session [1-tailed paired t -test, $t(11) = 1.86$; $P = 0.045$]. On the basis of this result, we entered the data from all ROIs into an ANOVA including the same factors as previously, with an additional factor of half (1st, 2nd). The main effect of half approached significance [$F(1,11) = 3.23$, $P < 0.1$]. All other previously reported effects remained significant. Although an intriguing finding, this issue deserves further investigation as we cannot rule out other possible causes for the increased responsiveness of visual cortex. We also note that the active control condition, which includes task-irrelevant tactile stimulation, shows a similar trend toward increased activation ($P < 0.1$).

DISCUSSION

We demonstrate that tactile processing in normally sighted, blindfolded subjects affects a network of visual cortical processing areas. Tactile task performance produced increased activation in V1 along with strong BOLD signal suppression in extrastriate areas, a pattern that appears inconsistent with the simple notion of cross-modal influences descending through a single hierarchical cortical network. These findings not only provide further evidence that *primary* sensory areas receive cross-modal input even in the intact brain but also suggest that at least two different tactile-visual pathways are implicated in cross-modal sensory processing.

The activation of primary visual cortex observed in the present study agrees with previous reports of calcarine activation during simple tactile discrimination tasks in individual sighted subjects (Burton et al. 2004, 2006; Weisser et al. 2005). Deactivation of occipital cortex during tactile tasks has also been previously observed (Kawashima et al. 1995; Sadato et al. 1996; Weisser et al. 2005). Here we extend these results by conclusively identifying in individual sighted subjects the visual areas modulated during tactile processing, demonstrating simultaneous activation of area V1 and suppression of extrastriate cortical areas.

Laurienti and coworkers have suggested that presenting unimodal stimuli will in general result in the cross-modal deactivation of nonmatching sensory areas. This deactivation of the unattended modality might result from either withdrawal of attention (Laurienti et al. 2002) or active attentional filtering. Consistent with this view, we observed a pattern of stronger

deactivation in higher visual areas, suggesting the existence of a hierarchical feedback pathway operating most strongly through the dorsal stream. The strong activation observed in the intraparietal sulcus, a region involved in both attention and multi-sensory processing (Roland et al. 1998), represents a potential source of this hierarchical feedback.

More puzzling is the activation of area V1. Although it is tempting to invoke cognitive explanations such as visual imagery and/or attention, these mechanisms seem unlikely. Subjects were not allowed to view the stimuli beforehand, discouraging the use of imagery. Moreover, activation of V1 due to imagery or attention typically occurs only in concert with stronger activation of extrastriate cortex (Kastner et al. 1998; Kosslyn and Thompson 2003; Slotnick et al. 2005; Somers et al. 1999), unlike the deactivation observed here. Disinhibitory mechanisms are inconsistent with the inter-areal correlations that we observed. Rather we interpret the activation of area V1 as reflecting the operation of a second, distinct neural pathway arising from outside the traditional visual cortical hierarchy. Our methods do not permit identification of the source of these direct inputs, but candidate sources include long-range cortico-cortical connections from multimodal parietal areas (Rockland and Ojima 2003), somatosensory processing areas, or other primary sensory cortices (Cappe and Barone 2005; Clavagnier et al. 2004; Falchier et al. 2002). Our results support the view that multisensory interactions within primary sensory areas are mediated by a competing balance between this form of direct drive and potentially inhibitory top-down projections from associative cortical areas.

The precise functional role of area V1 and surrounding extrastriate areas in tactile processing at this time remains unclear. One speculation is that cross-modal sensory integration in normal individuals occurs not only in higher-order multimodal cortical areas but also directly involves what has been traditionally thought of as unimodal sensory cortex (Schroeder and Foxe 2005). Prior TMS studies provide evidence for the functional relevance of these areas to tactile processing in normally sighted subjects (Merabet et al. 2004; Zangaladze et al. 1999). Merabet and coworkers (2004) delivered repetitive TMS (rTMS) pulses targeting primary visual cortex bilaterally, finding a selective disruption of inter-dot spacing determinations but not roughness judgments. In the present study, comparison of roughness and spacing tasks revealed greater activation during spacing judgments along the left (contralateral) intraparietal sulcus, appearing to overlap an area previously found to be more active in tactile judgments of shape than of surface roughness (Roland et al. 1998); however, no such task-specific effects were found in early visual areas. This suggests an apparent discrepancy between the prior rTMS results and the present fMRI study. It is possible that the effects of rTMS may be mediated transsynaptically, leading to selective disruption of remote task sensitive regions such as IPS. However, even in left IPS the task-specific effect was substantially smaller than the prominent task-general tactile activation. In V1, we found significant but weak task-general activation; it is likely that a smaller underlying task-specific effect in V1, as was observed in left IPS, simply could not be resolved in the present study. This is consistent with the small magnitude of the effect observed previously by Merabet et al. (2004).

Outside of early visual cortex, we found strong task-general activation along IPS, an area commonly reported to be active

during tactile processing (Amedi et al. 2002; Prather and Sathian 2002; Stoesz et al. 2003; Van Boven et al. 2005; Weisser et al. 2005; Zhang et al. 2005). An additional smaller locus of activity in ventral occipital/inferior temporal cortex was also observed. Although visual object processing regions have not been independently localized in these subjects, this ventral activation appears to lie in close proximity to visual cortical areas previously reported to be involved in tactile object recognition (Amedi et al. 2001, 2002; James et al. 2002; Pietrini et al. 2004; Prather and Sathian 2002; Reed et al. 2004; Stoesz et al. 2003). Previous studies have shown tactile activation of area MT+ during processing of moving or vibrating tactile stimuli (Burton et al. 2004; Hagen et al. 2002; Moore et al. 2005). In contrast, we observed MT+ to be deactivated in all six subjects in whom this region was individually localized. This lack of MT+ activation may be due to the fact that all tactile motion in the present study was self-produced rather than being externally imposed. Self-generated tactile motion (active touch) has been shown to lead to reduced cortical activation relative to external motion (Blakemore et al. 1998), although this distinction did not affect behavioral performance in a similar task (Vega-Bermudez et al. 1991). The areas of strong deactivation we observed outside of occipital cortex included many regions that are commonly found to be deactivated during attentionally demanding tasks (Binder et al. 1999; Fox et al. 2005).

The finding of activation in primary visual cortex during tactile stimulation in sighted subjects supports the hypothesis that enhanced cross-modal connectivity following profound sensory deprivation (Wittenberg et al. 2004) may be derived from preexisting sensorimotor processing networks found in the intact brain (Burton et al. 2004). It is likely that the same multimodal networks implicated in normal cross-modal sensory processing (Calvert 2001; Macaluso et al. 2000; Schroeder and Foxe 2005) are dramatically altered and expanded under the demanding conditions after sensory loss (Pascual-Leone et al. 2005). In the blind, activation of both striate and extrastriate areas has been reported during tactile processing (e.g., Burton et al. 2004, 2006). Here we demonstrate that in the sighted, striate activation is combined with extrastriate suppression. The positive correlation between activity levels in V1 and the extrastriate areas suggests that these areas remain functionally connected during tactile processing. Furthermore, we find a trend toward increased activation throughout visual cortex over the course of the scan session, consistent with an increase in occipital excitability (Boroojerdi et al. 2000) or an initial phase of rapid plasticity (Weisser et al. 2005) in response to short-term visual deprivation. This is consistent with the hypothesis that long-term visual deprivation could lead to a reversal of the extrastriate deactivation observed here. These results provide further support for the emerging view that cross-modal influences are present even at the earliest cortical stages of the intact visual system.

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