Neocortical Correlates of Vibrotactile Detection in Humans

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Abstract

■ This study examined the cortical representation of vibrotactile detection in humans using event-related fMRI paired with psychophysics. Suprathreshold vibrotactile stimulation activated several areas, including primary (SI) and second somatosensory cortices (SII/PV). For threshold-level stimuli, poststimulus activity in contralateral and ipsilateral SII/PV was the best correlate of detection success. In these areas, evoked signals on hit trials were significantly greater than on missed trials in all participants, and the relative activity level across stimulation amplitudes matched perceptual performance. Activity in the anterior insula and superior temporal gyrus also correlated with hits and misses, suggesting that a "ventral stream" of somatosensory representations may play a crucial role in detection. In contrast, poststimulus activity in Area SI was not well correlated with perception and showed an overall negative response profile for threshold-level stimulation. A different correlate of detection success was, however, observed in SI. Activity in this representation immediately before stimulus onset predicted performance, a finding that was unique to SI. These findings emphasize the potential role of SII/PV in detection, the importance of state dynamics in SI for perception, and the possibility that changes in the temporal and spatial pattern of SI activity may be essential to the optimal representation of threshold-level stimuli for detection. ■

INTRODUCTION

The detection of tactile stimuli is a fundamental perceptual goal and has a long history of study. Previous reports that have investigated tactile detection or employed threshold-level stimuli have largely emphasized evoked activity in primary somatosensory cortex (SI) and generated ambiguous findings. Threshold and subthreshold stimuli evoke electrophysiological responses in primary somatosensory cortex (SI; Jones et al., 2010; Jones, Pritchett, Stufflebeam, Hamalainen, & Moore, 2007; de Lafuente & Romo, 2005; Palva, Linkenkaer-Hansen, Näätänen, & Palva, 2005; Linkenkaer-Hansen, Nikulin, Palva, Ilmoniemi, & Palva, 2004; Mountcastle, Talbot, Sakata, & Hyvarinen, 1969; Libet, 1967). Lesion studies in humans show deficits in thresholds for the detection of von Frey filaments (Corkin, Milner, & Rasmussen, 1964), and lesions in macaque monkeys show that activation in this region is essential for transmission to higher cortical areas (Pons, Garraghty, & Mishkin, 1992).

These findings suggest that SI would play a role in detection, a prediction supported by studies of the SEP. Studies in monkeys have reported that the amplitude of the SEP in or above the postcentral gyrus (PoCG) is positively correlated with detection (Kullics, 1982). Magnetoencephalography (MEG) signals localized to the posterior bank of the central sulcus (the fingertip representation in Area 3b) show that changes in the SI-evoked response predict tactile detection (Jones et al., 2007; see also Palva et al., 2005). Furthermore, prestimulus oscillatory activity also strongly correlate with hits and misses, with higher power in the alpha and beta bands both negatively related to perceptual success (Jones et al., 2010; Linkenkaer-Hansen et al., 2004).

These studies are in contrast with action potential recordings and lesion data in well-trained monkeys. Using single-unit recording techniques in the macaque, de Lafuente and Romo (2005) found that changes in the evoked firing rate of quickly adapting neurons in SI did not correlate with detection of a vibrotactile train. This finding is consistent with other reports using single unit recording in monkeys (Hyvärinen, Poranen, & Jokinen, 1980; Carli, LaMotte, & Mountcastle, 1971; see also Ageranioti-Belanger & Chapman, 1992; Chapman & Ageranioti-Belanger, 1991). Furthermore, lesions of SI in monkeys leads to mild and often reversible impairments in detection capability (Zainos, Merchant, Hernandez, Salinas, & Romo, 1997; Knecht, Kunesch, & Schnitzler, 1996; LaMotte & Mountcastle, 1979). Furthermore, the negative impact of SI lesions in humans on detection, although measurable, is not complete (Corkin et al., 1964).

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In contrast to these SI findings, prior studies suggest that activity levels in higher cortical representations do correlate with detection probability. Using the same paradigm applied during SI recording, de Lafuente and Romo (2005) found that firing rate in the medial premotor cortex tracked hits and misses at threshold. Recent studies using magneto-encephalography have shown that evoked potentials recorded on sensors over the parietal operculum show predictive differences on hits and misses (Palva et al., 2005). This finding suggests that the second somatosensory cortex (SII/PV) plays a role in detection but is inconclusive as to the precise representations engaged, as the region recorded by these sensors likely contains four or more somatosensory representations in the human (Eickhoff, Schleicher, Zilles, & Amunts, 2005; Disbrow, Roberts, & Krubitzer, 2000).

To investigate the processing of vibrotactile detection, we combined event-related fMRI with perceptual performance. This approach allowed the delineation of multiple cortical areas, and the relation of activity in these areas to detection success. Perhaps most importantly, this non-invasive method permitted the association of perception and activity in the normal human subject. We observed a consistent association between detection probability and activity in SII/PV and insular and temporal regions, suggesting that a ventral stream of tactual areas, defined by anatomical position, is central to this task. In contrast, activity in SI showed negative fMRI signal at threshold and did not consistently correlate with detection success. However, SI signal before stimulus onset predicted perceptual performance, with lower baseline activity levels predicting misses and higher baseline levels predicting hits. These findings provide specific hypotheses as to cortical areas that are crucial to detection success and the divergent coding mechanisms that may be engaged in SI and SII/PV.

METHODS

Participants and Scanning Parameters

Participants ($n = 7$; age = 24–31 years; five women; all right-handed) were scanned in a 3T Siemens head-only system with a birdcage head coil. All participants granted informed written consent, and all experiments were conducted in accordance with an approved Massachusetts General Hospital protocol for human studies. Functional data (21 slices; $3.125 \times 3.125 \times 4$ mm voxel size, 0.8 mm skip, repetition time = 2000 msec, echo time = 30 msec) were acquired in the horizontal oblique plane approximately orthogonal to the course of the central sulcus.

Study Design

A scanning session consisted of ten 6-min runs, in which 520 trials were presented. Each trial lasted 4 sec (Figure 1A). To delineate the event-related time course, a 0–12 sec intertrial interval was imposed between the onset of successive trials. The event-related presentation schedule was optimized for the number of trial types and the distribution of intertrial intervals presupposing a linear time-invariantsystem with additive Gaussian noise (Dale, 1999). Furthermore, the order of presentation of the 10 scans was counterbalanced across subjects.

Within the 520 trials in each single experiment, 12 trial conditions were presented (Table 1). Trials varied in task demand, the frequency and amplitude of vibrotactile stimulation, and the requirement of a psychophysical report via motor response. To investigate the cortical correlates of vibrotactile detection, the analysis presented here is focused on those trials with psychophysical report. Throughout the experiment, during trials and intertrial intervals, participants fixated a small "+" sign in the center of the visual field, projected onto a silvered mirror using an LCD projector (Sharp model XG-NV6XU, Mahwah, NJ). For 11 of 12 conditions, a trial initiated when a colored rectangle appeared superimposed on the fixation point, followed 1 sec later by a 1-sec duration vibratory stimulus of varying amplitude. For "overt" responses where a psychophysical response was required, the visual cue was green, and subjects indicated the perceived presence or absence of tactile stimulation by a button press with the right hand following cessation of the visual stimulus (second digit press for present, third digit for absent; Figure 1A). For "covert" responses, a red rectangle was presented, and subjects were required to perform the task without providing button-press report. On the 12th trial type, the "no task" condition, a 100-Hz 1-sec duration stimulus was presented without prior visual cue, and subjects were not required to make covert or overt responses.

Tactile Stimulation

Tactile stimuli were administered by a piezoelectric bimorph with brass shim (2.5×1.25 in., #503; Piezo Systems, Woburn, MA). The piezoelectric was driven through custom amplifiers that delivered a voltage across two customized copper plates, one on each side of the base of the piezoelectric, covering its full width and one-half its length. The output signals (20 or 100 Hz sinusoids) driving the piezoelectric were generated using custom programs (MATLAB) and delivered through an eight-output sound card using accompanying software that also controlled visual stimulus presentation (ARC88, Sek'd, Woburn, MA). The copper plates were pinned to the two sides of the piezoelectric by a top plate and base made of delrin, both milled to precisely fit the piezoelectric and copper plate dimensions. The delrin surface plate was connected to its base by six adjustable screws that ensured a balanced contact between copper and piezoelectric. This holding arrangement was in turn housed in a custom nonmagnetic manipulator with displacement control in the vertical dimension. Participants rested their arms on a cushioned ramp and placed their hands on a custom delrin stage (adjustable for height and angle) with a shallow convex palm support.

Figure 1. Detection paradigm, activated regions, and time course of activity in areas SI and SII/PV. (A) The tactile detection paradigm. On trials with perceptual report, participants were visually cued with a green rectangle ("Visual") 1 sec before the onset of a 1-sec vibrotactile stimulus ("Tactile"). The visual stimulus then persisted 1 sec after the cessation of the tactile input, and participants made a button press to indicate the detection or nondetection of a stimulus ("Motor"). (B) An inflated cortical representation from a single participant, showing for this individual the contralateral regions that were activated by suprathreshold tactile stimulation across subjects. Abbreviations in the boxes are discussed in the text. Numbers correspond to the following: 1 = ventral premotor cortex; 2 = posterior STG superior; 3 = posterior STG inferior; 4 = anterior superior temporal sulcus; 5 = anterior insula; 6 = posterior insula. (C) Averaged activity (*n* = 7 participants) in SI and SII/PV evoked by full amplitude stimulation in the 20 Hz "Overt" detection condition (black lines) is contrasted with activation evoked by the "No Task" tactile-only condition that was presented without a visual cue or associated button press (full amplitude 100 Hz stimulation; gray lines). For

data presentation throughout, the factor determined by multiple regression to be the baseline level of activity was referred to as "0%" and change in activity expressed in percent signal change. Areas SI and SII/PV showed similar evoked tactile signal in response to tactile stimulation during the task and the non-task stimulation, peaking 3 sec after stimulus onset (gray background).
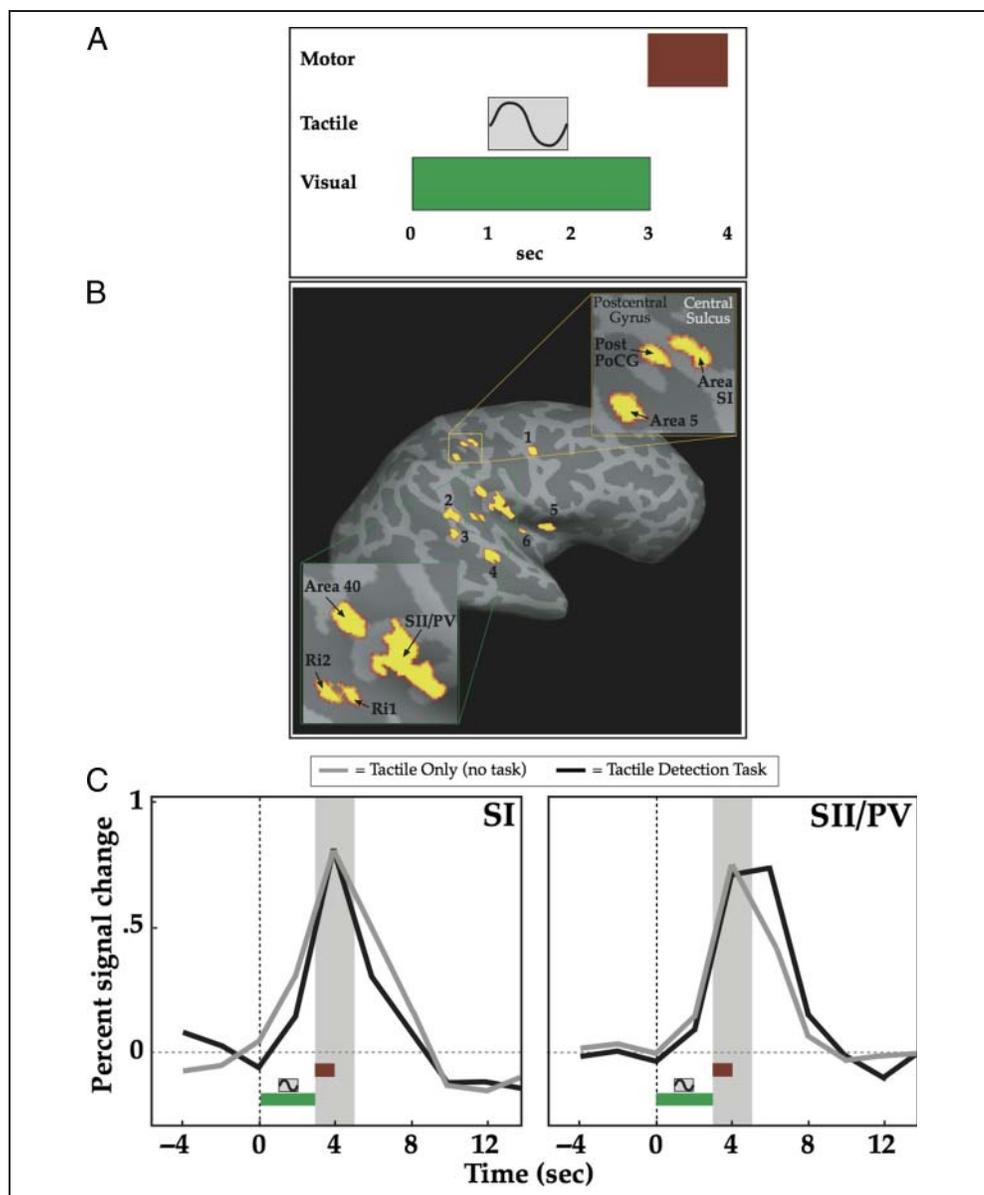
Table 1. Distribution of Trial Conditions

	20 Hz "Covert"	100 Hz "Covert"	20 Hz "Overt"	100 Hz "No Task"
200 μm tactile stimulation	40	40	40	80
100 μm	40	40	40	
20 μm ("threshold" @ 20 Hz)	40	40	40	
No stimulation		40		40

The distribution of different trial types administered is shown. "Overt" and "Covert" refer to whether detection was reported by button press or whether the task was performed but no response given, respectively. "No Task" indicates that a stimulus was presented, but no response was required. In each cell, the number of trials of a given type presented during an experiment in a single subject is indicated (of 520 total). Blank cells indicate that no trial of that type was presented.

Contact with the skin of the distal segment of the third digit of the left hand was made with a delrin attachment threaded into a holder attached to the piezoelectric. The tip of the contact probe had a ~3.5 mm inner diameter/ 6 mm outer diameter beveled-edge circular contact surface with a ~33° taper. Stimuli were presented through a 1-cm-wide rigid plastic slot oriented perpendicular to the long axis of the finger, the inner diameter of the contact surface positioned level with the surround. Auditory cues from the piezoelectric stimulator, which were typically negligible, were masked by headphones, foam padding around the head, and ongoing scanner noise.

The tactile stimulus amplitudes employed in the scanner were chosen based on a prior study of detection thresholds conducted using the same stimulator and an independent group of participants outside the scanner (data not shown; $n = 6$ participants). The 20-µm deflection amplitude at 20 Hz was selected, based on this previous

study, as a stimulation level that evoked a predominance of "hits" (the correct detection of a presented stimulus) and a significant fraction of "misses" (the failure to detect a presented stimulus). This rate of detection was similarly observed during perceptual testing in the scanner environment, as described in Results and shown in Figure 2. On the basis of this distribution of responses, the 20-Hz/20-µm trial condition is referred to throughout as "threshold."

Data Analysis

Identification of Activated Cortical Areas

The cortical surface was reconstructed and registered with high-resolution scans (SPGR 128 slice, 1.0 cubic mm) acquired in a separate session (Fischle, Sereno, & Dale, 1999). Motion correction (AFNI) was conducted and signal
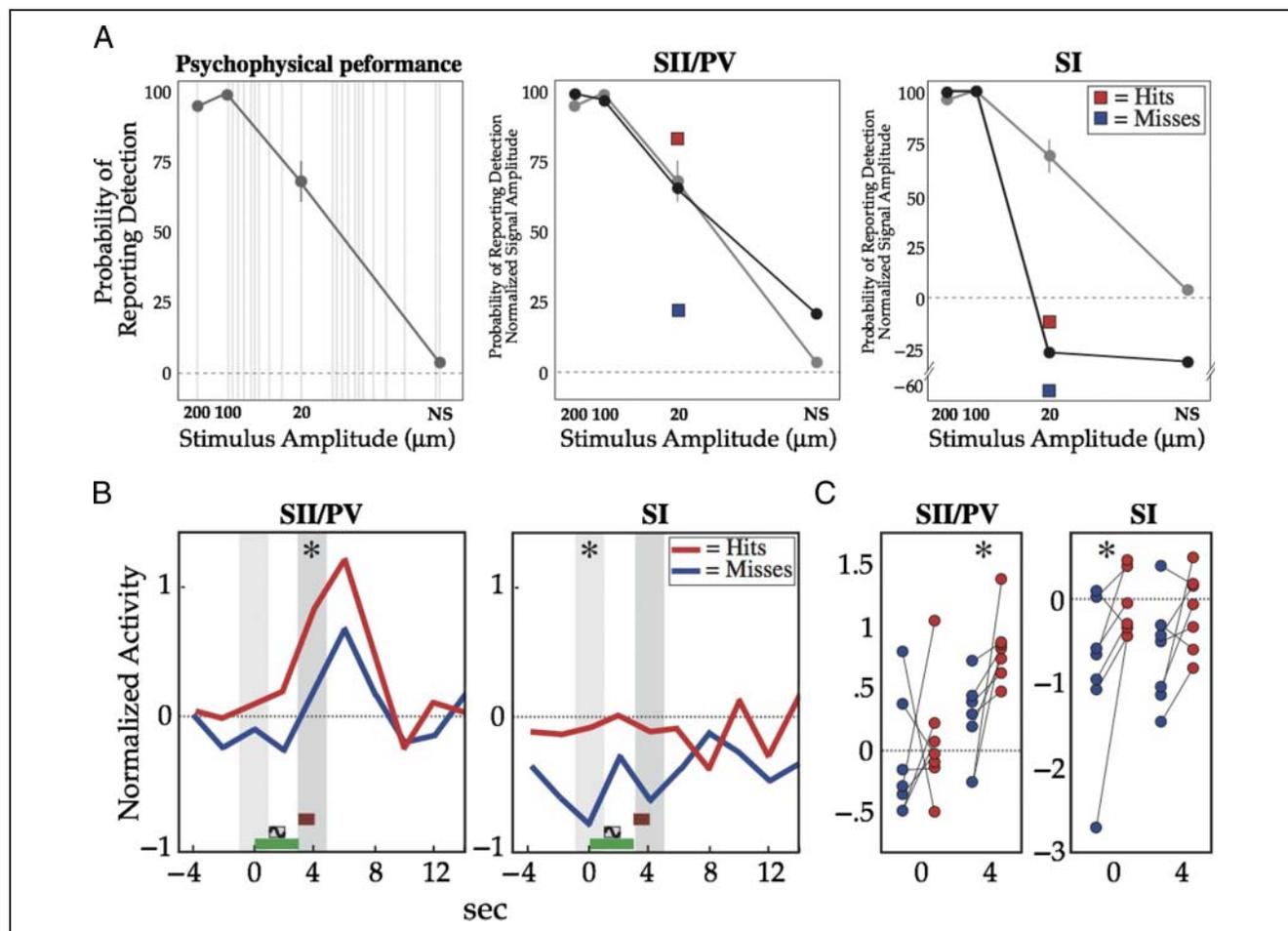
Figure 2. Psychometric curves, activation functions, and time courses on hit and miss trials for areas SI and SII/PV. (A) Left graph: Psychophysical performance during scanning, average ± *SEM* across all seven participants. Center and right graphs: Comparison of fMRI activation (black lines) and psychometric performance (gray lines) as a function of stimulus amplitude. Square symbols show the mean evoked signal change during hit (red) and miss trials (blue) at threshold. (B) Hit and miss time courses at threshold averaged across participants ($n = 7$). Significant differences, indicated by an asterisk, were observed in SI activity immediately before vibrotactile stimulation and in evoked SII/PV activity ~4 sec after trial onset. (C) Scatter plots showing activity for each participant during the baseline period at the onset of the trial ("0 sec") and during the evoked activity period ("4 sec"). Lines connect data within single participants for miss (blue circles) and hit trials (red circles).

was globally normalized. Following selective averaging and response deconvolution, activation maps were determined using an F test to compare evoked signal to the residual error 3 sec after tactile onset (Figure 1C; Burock, Buckner, Woldorff, Rosen, & Dale, 1998). In each participant, cortical areas responsive to tactile stimulation were defined by analyzing the signal evoked by the four stimulus trial types that employed 200-µm stimulation amplitude, the maximal stimulus applied (the "omnibus" analysis). These conditions were covert detection of 20 and 100 Hz stimuli, overt detection at 20 Hz, passive stimulation at 100 Hz, a total of 200 trials (Table 1). A two-step procedure was then employed for the delineation of cortical areas that would be further analyzed. First, a statistical threshold was applied in individual participants to delimit significant activity 3 sec post-vibrotactile stimulus onset ($p < .00001$). Second, regions activated in at least six of seven subjects (sign test, $p \leq .06$) and that showed a significant signal increase in response to the tactile only condition were further analyzed. Use of a more restrictive criterion at the second analysis stage, requiring activation in all seven of seven subjects ($p \leq .008$), would have excluded Area 40, the posterior insula, the first and second retroinsular areas, the ipsilateral superior temporal gyrus (STG), and the ipsilateral posterior inferior temporal sulcus from further analysis. Beyond this observation, we did not investigate the impact of thresholding procedure on which areas would have been analyed.

Analysis of the Relation between Perceptual Report and Activation

In each area, we evaluated the relation between evoked activity and detection by assessing three criteria: (1) whether activity during hit trials at threshold could be dissociated from activity during miss trials, (2) whether activity during hit trials at threshold could be dissociated from activity during no stimulation trials, and (3) presuming a linear correspondence between perception and activation levels (Romo & Salinas, 2001; Parker & Newsome, 1998; Johnson, Hsiao, & Blake, 1996; Mountcastle, 1967), whether the shape of the activation function matched the psychometric function. The first and second criteria for association between activity and psychophysical performance (hits vs. misses and hits vs. no stimulation, respectively) were evaluated in two ways. First, a two-tailed t test ($p \leq .05$) was performed for activity evoked by hits versus misses in the threshold condition or by hits (at threshold) versus no stimulation within each individual. A sign test was then applied to determine if a significant number of individuals ($n = 6/7$; $p \leq .06$) showed greater activity on hit trials in that area. Second, as a complimentary nonparametric analysis, a Wilcoxon test was employed to compare mean signal change across subjects for hits versus misses and hits versus no stimulation ($p \leq .05$). These methods were applied to prestimulus and poststimulus evoked activity.

To assess the third criterion, similarity between the psychometric and activity functions, we calculated the correlation coefficient between the slopes for the three segments of the activity and psychometric functions across subjects. To enable this third analysis and to permit the averaging of activation functions across participants, the response in each area was normalized to the signal evoked by full-amplitude stimulation (20 Hz/200 µm). We selected this approach over two other normalization schemes, normalization of evoked activity to the no stimulation activity level and simultaneous normalization to the maximal amplitude stimulus response level and to the no stimulus level. Normalization to the no stimulation condition proved inappropriate because activity during no stimulation was often negative. Furthermore, this analysis was susceptible to noise, as small differences in activity around 0% signal change led to substantial variation in the normalized peak signal change across subjects. The second approach, constraining both the peak and no stimulation levels, removed important features of the data. This analysis distorted interpretation of activity in areas where tactile amplitude-independent activity predominated, most notably areas putatively associated with the motor performance aspect of the task (e.g., Figure 3B).

RESULTS

Areas Activated by Event-related Vibrotactile Stimulation

Event-related tactile stimuli evoked activation in multiple contralateral areas in all participants ($n = 7$; see Methods; Figure 1B). In the PoCG, a dual representation of the fingertips was observed, with one activation region in the anterior PoCG (SI) and a second immediately posterior to it (posterior PoCG; Figure 1B, top inset). Monkey electrophysiological and anatomical data and human imaging and cytoarchitectonic data suggest that the anterior region observed in this study corresponds to the fingertip representation of Area 3b, regarded as "SI," and the posterior region to bordering fingertip representations of Areas 1 and 2 (Moore et al., 2000; Geyer, Schleicher, & Zilles, 1999; Burton, Macleod, Videen, & Raichle, 1997; Pons, Garraghty, Cusick, & Kaas, 1985; Kaas, 1983; Merzenich, Kaas, Sur, & Lin, 1978).

In the parietal operculum, a region that likely overlapped the finger representations of two distinct areas, SII and the parietal ventral area, was also activated (SII/PV; Figure 1B, bottom inset; Eickhoff et al., 2005; Disbrow et al., 2000; Krubitzer, Clarey, Tweedale, Elston, & Calford, 1995). Several other putative somatosensory cortical areas were recruited, including Area 5, Area 40, two areas in the retro-insular cortex, and two areas more anterior within the insula (Figure 1B and Table 1; Downar, Crawley, Mikulis, & Davis, 2000; Coghill et al., 1994; Friedman, Murray, O'Neill, & Mishkin, 1986; Robinson & Burton, 1980; Mountcastle, Lynch, Georgopoulos, Sakata, & Acuna,

Figure 3. Activation functions for all driven cortical areas. Areas were segregated into three general categories based on the similarity between the psychometric and activity functions at threshold. On all graphs, the psychometric function is shown in black. (A) Areas with normalized signal change at threshold that fell within the standard error of the psychometric function. (B) Areas with signal greater than the psychometric function at threshold. These areas ostensibly participate in the task-related aspects of detection, including motor control of the button press, in addition to being driven by isolated tactile stimulation. (C) Areas with signal lower than the psychometric function at threshold. The lower responses were further subdivided into (i) areas without a significant difference between hit and no stimulation activity and (ii) areas with an apparently linear fall-off in signal amplitude, similar to those in A, but that did not meet any of the criteria for association with psychophysical performance (Table 2).
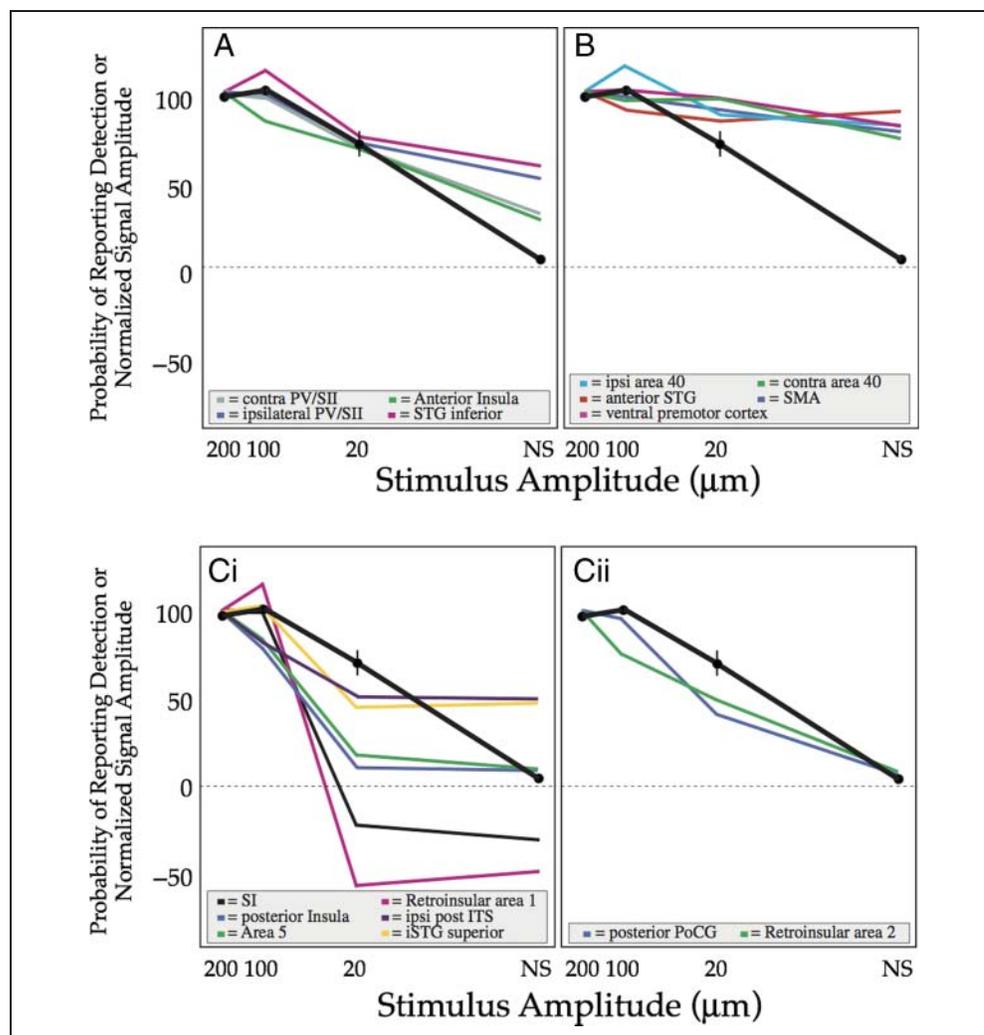
1975). Four additional areas were consistently recruited in the ipsilateral hemisphere, Area SII/PV, Area 40, the middle STG, and the ipsilateral posterior inferior temporal sulcus.

Psychophysical Performance

Psychophysical performance during fMRI scanning was consistent across subjects (Figure 2A). All participants (*n* = 7) showed a 92% hit rate or higher for stimuli applied at 200 or 100 μm at 20 Hz, with average rates of 96 ± 4% (*SD*) and 99 ± 1%, respectively. Similarly, participants accurately reported the absence of a stimulus, with a false positive rate of less than 12% in all subjects and an average rate of 4 ± 4%. In the "threshold" condition (20 μm stimulation), six of seven participants had hit rates between 65% and 81% correct, with one participant at 30%, and an average rate of 65 ± 17%.Although this study was not designed to look at the impact of previous trial intervals on subsequent detection, a limited analysis indicated no systematic influence of this factor on the probability of a miss. Across all intertrial intervals measured, a less than 3% dif-

ference existed between the base probability that a given interval would precede a threshold stimulus and the probability that such an interval would precede a miss. Similarly, fatigue during a scanning session did not appear to impact detection probability. Of all missed trials, 13.4% occurred during the first scan a participant performed, and 7.3% during the final scan, where 10% of misses is predicted to occur in each of the 10 scans.

Relation of Evoked Activity in Areas SII/PV and SI to Detection

In all participants (*n* = 7), the evoked activity in SII/PV for hits (0.82 ± 0.28% *SD*) was greater than for misses (0.23 ± 0.35%: Figure 2A, B, first panel; Table 2), and all participants showed greater signal for hits (at threshold) than for no stimulation. Furthermore, signal change in SII/PV during performance of the task was significantly correlated with the psychometric function for detection probability (Table 2). Normalized activity evoked in contralateral SII/PV by the 100-μm stimulus was 0.97 (97% of the response evoked by the maximal stimulus), a value similar to the

Table 2. Cortical Areas Activated by Vibrotactile Stimulation and Their Relation to Detection

Area	Talairach Coordinates			Criteria for Association between Activity and Probability of Detection				
	x	y	z	t H v M	W H v M	t H v NS	W H v NS	r
SII/PV	53.3	−20.3	22.4	■	■	■	■	■
Ipsilateral SII/PV	−61.0	−17.2	21.6	■	■	■	■	■
Anterior insula	36.6	−3.7	13.1	■	■		■	■
STG inferior	59.0	−42.9	11.0	■	■			■
Ventral premotor cortex	50.2	1.0	46.1			■	■	■
Anterior STG	55.5	−22.3	−5.7	■	■			
Ipsilateral area 40	−62.6	−26.6	27.3			■		
Area 40	57.5	−27.3	27.7					
SI	48.8	−25.3	61.5					
Posterior PoCG	51.1	−29.1	57.7					
Area 5	51.9	−23.7	46.2					
Retroinsular area 1	43.9	−36.6	19.4					
Retroinsular area 2	49.1	−36.5	20.1					
Ipsilateral STG superior	63.7	−36.8	20.7					
Posterior insula	37.3	−23.0	4.8					
SMA	9.2	3.6	56.6					
Ipsilateral posterior inferior temporal sulcus	−43.1	−66.7	3.5					

Left-hand column: The cortical areas activated by suprathreshold tactile stimulation. Center column: The Talairach coordinates for these areas averaged across subjects. Right-hand columns: Filled cells indicate that a statistically significant effect was observed for the corresponding criterion in that cortical area (see Methods for details). Blackened cells demarcate the area with the highest value within that category (e.g., highest correlation coefficient). The following abbreviations apply: "H v M" denotes hit versus miss comparisons and "H v NS" denotes hit versus no-stimulation comparisons; "t" indicates t-test-based comparisons; and "W" indicates Wilcoxon comparisons; "r" indicates correlation coefficient.

detection probability of 99% correct, and the signal evoked by threshold-level (20 μm) stimulation was 0.62, comparable to the 65% detection rate. Across all cortical areas and all analyses applied, signal in SII/PV best reflected probability of detection (Table 2). A parallel pattern of activity was observed in ipsilateral SII/PV, the only other area to meet all of the applied criteria.

Activity levels in SI tracked basic changes in stimulus amplitude. Larger stimuli (200- and 100-μm amplitude) evoked greater signal than smaller stimuli (20-μm amplitude), in agreement with previous monkey and human studies (Figure 2B, second panel; Nelson, Staines, Graham, & McIlroy, 2004; Mountcastle & Powell, 1959). However, in contrast to SII/PV, evoked signal in SI did not track perceptual capability at threshold. A trend toward separation between hits and misses existed in SI, with hits at threshold (−0.11 ± 0.47%) greater than misses (−0.62 ± 0.63%), but these trends failed to meet any of the applied criteria for the association of activation and detection probability (Table 2). Furthermore, activity during threshold-level stimulation was net negative relative to the global baseline and was not significantly different from activity during no stimulation.

To test whether variation in individual hemodynamic response functions could account for this null result in SI, we identified the latency to the first significant activation and the latency to the initial peak activation in each subject for the "omnibus" analysis. The latency to initial activation in SI was evenly divided across participants: In three of seven participants, significant SI activation was observed in the first time point poststimulus, "1 sec" after tactile onset. Although this response latency is brief, it likely reflects the fact that time points shown represent activity sampled at discrete times within a 2-sec window following the assigned time point, following standard labeling conventions. As such, "1 sec" poststimulus reflects activation from 1–3 sec poststimulus onset. In four of seven subjects, the first significant activation was observed 3 sec (i.e., 3–5 sec) post-trial onset. Peak activation, in contrast, was largely observed at a single time point: In six of seven subjects, peak activation occurred 3 sec poststimulus onset, as suggested by the average response properties in Figures 1 and 2, and in one participant, it occurred 1 sec poststimulus onset. Having identified the onset and peak of activation in each participant, we then applied the set criteria to each. We also analyzed activation 1 and 5 sec

poststimulus onset, the time points bracketing the time point employed in our initial analysis. Despite tailoring our analysis to participant-specific variation in the hemodynamic signal and broadening the time points examined, none of these further analyses of SI met any of the criteria for association between perceptual behavior and poststimulus activity.

Relation of Ongoing Activity Level to Detection

In addition to analyses relating the evoked response to signal detection, we also examined how ongoing activity at the time of trial onset, the "state" properties of an area, predicted detection success. Although evoked activity in SI was not a consistent indicator of detection probability, activity in SI immediately before vibrotactile stimulus onset tracked perception. In six of seven participants, activity during the baseline period before hits was greater than activity before misses, and the mean activity levels at stimulus onset were significantly different (Figure 2; hit trials = −0.07 ± 0.38% vs. miss trials = −0.81 ± .95%; $p < .05$, Wilcoxon test). Of the 18 areas analyzed, SI was the only region to show a significant predictive baseline activity level for hit and miss trials. Furthermore, to the extent that SI showed a trend toward dissociation of hits and misses in activity poststimulus onset, this difference appears to be best described as the consequence of a prestimulus bias in the level of ongoing activity on hit and miss trials that was sustained through the evoked activity period (Figure 2C).

Stimulus-related Activation Functions across Cortical Areas

The pattern of signal change in activated cortical areas fell into three general categories, segregated for presentation by correspondence between the activity and psychometric functions at threshold. The first category is shown in Figure 3A and includes contralateral and ipsilateral SII/PV, the anterior insula, and the inferior bank of the STG. These areas were selected for presentation by having activity functions that were within the standard error of the psychometric function at 20-μm stimulation amplitude. All of these areas also showed a significant dissociation between activity evoked on hit and miss trials. These two kinds of measures (similarity between activity functions and psychometric functions and the dissociation of hits vs. misses) were independent criteria, and their convergence suggests that these areas play a specific role in the detection of vibrotactile stimuli.

In contrast to the areas shown in Figure 3A, the relative activity levels in other cortical areas failed to track the psychometric function (Figure 3B, C). Areas typically associated with motor planning or execution (e.g., SMA and ventral premotor cortex; Figure 3B) showed activity levels that exceeded the psychophysical prediction, pre-

sumably due to the consistent requirement for a motor output independent of tactile stimulus content. Areas that fell below the psychometric prediction were segregated into two categories: Those that showed no apparent signal increase at threshold (e.g., Area SI; Figure 3Ci) and those that showed an approximately linear decrease with tactile signal intensity (e.g., the posterior PoCG; Figure 3Cii). Although this second category of areas possessed activity functions that more closely matched variation in the amplitude of tactile stimuli presented, none of them showed a consistent correspondence between evoked activity and performance when the three kinds of criteria were applied (Table 2). Only the ventral premotor area met even half of the five analyses applied, and this region did not demonstrate a difference in the amplitude of evoked activity for hits versus misses.

DISCUSSION

In this study, we observed distinct correlates of tactile detection success in SI and SII/PV. The evoked activity level in SII/PV and a subset of ventral cortical areas distinguished hits from misses at sensory threshold. These findings suggest that a net increase in neural activity in these areas, reflected in the fMRI signal, is a determinant of detection success. Whereas poststimulus activity in SI did not map to detection success, prestimulus activity in this region did, suggesting that the state properties of SI and neural codes other than increases in the net level of neural activity are important in tactile stimulus detection. This double dissociation of detection correlates in these key somatosensory representations presents specific hypotheses as to the signals that are crucial for this fundamental behavioral capacity.

Evoked Activity in SII/PV and a Ventral Stream of Cortical Areas Predict Detection

The findings presented here argue strongly for the specific relevance of Area SII/PV in the detection of vibrotactile stimuli. Changes in signal amplitude in SII/PV for hits and misses accurately tracked detection behavior at threshold in all subjects. Furthermore, the activity function in SII/PV across all amplitudes was better correlated with the perceptibility of the stimulus than with the amplitude of the stimulus. The response levels for all suprathreshold stimuli, including 200- and 100-μm stimulation and hit trials at threshold, were similar. This finding in SII/PV is in agreement with Nelson and colleagues (2004), who also observed no distinction in the amplitude of SII activity within the category of suprathreshold stimulation. Similarly, the response level for miss trials at threshold in SII/PV was similar to that observed for no stimulation.

The discriminative value of evoked SII/PV activity in vibrotactile detection corresponds well with the activation of this area by vibratory and textured surfaces in

humans and monkeys (Roland, O'Sullivan, & Kawashima, 1998; Burton et al., 1997; Seitz & Roland, 1992), the robust attentional modulation of this region in humans and monkeys (Nelson et al., 2004; Steinmetz et al., 2000; Burton, Videen, & Raichle, 1993; Hsiao, O'Shaughnessy, & Johnson, 1993; Poranen & Hyvarinen, 1982), and with its central anatomical interconnectivity in the nonhuman primate (Friedman et al., 1986). These findings are also in agreement with MEG recordings over the parietal operculum that have shown larger amplitude responses on hit trials for the detection of an electrical stimulus (Palva et al., 2005).

Temporal and insular areas also showed a close association between evoked activity and detection success. The anterior insula demonstrated a significant association between evoked signal change and psychophysical performance on most metrics applied, a finding that corresponds well with the activation of this region by variation in the quality of ongoing perceptual input (Downar et al., 2000). The inferior bank of the STG also met criteria for dissociating hits versus misses, although this region failed to show significance for the dissociation of hits and no stimulation. The activity patterns in SII/PV and in these regions suggest that a somatosensory ventral stream is important in making judgments of vibrotactile detection (Roland et al., 1998; Friedman et al., 1986; Mishkin, 1979), in contrast to a posterior parietal flow of information associated with macrogeometric or tactile motion perception (Bremmer, Schlack, Duhamel, Graf, & Fink, 2001; Roland et al., 1998).

The present findings also showed moderate but not complete agreement with single-unit recordings in the macaque premotor cortex during tactile detection (de Lafuente & Romo, 2005). In this study, premotor cortex was robustly activated by tactile stimulation, and the pattern of premotor activity met three of the five applied criteria for association between signal change and tactile perception. However, activity in premotor cortex evoked by hits versus misses was not significantly dissociated, in contrast to the robust differences seen in contralateral and ipsilateral SII/PV. These differences in the premotor cortex may reflect differences between the neural representations present in highly trained monkeys as contrasted with those in normal human participants and/or a dissociation of the action potential activity of neurons and fMRI signal.

As indicated in Figure 3 and in the above discussion, we emphasize that we attempted to understand both the correspondence between BOLD activity levels and perception (i.e., psychophysical capability; e.g., Figures 2 and 3A) and BOLD activity levels and overall intensity of stimulation applied to the skin (e.g., Figure 3Cii). Obviously, the BOLD signal itself is not neural activity. Although we have argued that this hemodymic signal may play a role in information processing (e.g., Moore & Cao, 2008), the correlations between patterns of neural activity and the BOLD signal are still only poorly understood. Furthermore, although correlations have been found between spiking and subthreshold indicators in specific neuron types, only recently have the precise causal methods been brought to bear in studying this problem required for fully understanding BOLD origins (e.g., Kahn et al., 2011).

"Evoked" Activity in Area SI

In Area SI, we observed a general agreement between stimulus amplitude and evoked activity, with larger, suprathreshold stimuli evoking greater responses than threshold-level stimuli. We did not, however, observe significant activation in SI at threshold, with a net decrease in post-stimulus response amplitude at this stimulus level, an effect driven primarily by lower values on subliminal, missed trials (Figure 3). This finding is in agreement with Blankenburg et al. (2003), who also reported a negative fMRI signal change in the contralateral SI hand area for responses to subliminal stimuli. Focal decreases in blood flow have also been observed in the ipsilateral SI hand representation during suprathreshold tactile stimulation (Hlushchuk & Hari, 2006).

These fMRI data are in contrast with a variety of electrophysiological recording approaches that have reported signals in SI in humans and monkeys for threshold-level and subliminal stimuli, including both field potential (Jones et al., 2007, 2010; Palva et al., 2005; Kullics, 1982; Libet, Alberts, Wright, & Feinstein, 1967) and suprathreshold action potential activity (de Lafuente & Romo, 2005; Hyvärinen et al., 1980; Carli et al., 1971; Mountcastle & Powell, 1959). This dissociation between hemodynamic and neural responses in SI may occur through several mechanisms. One hypothesis is that subliminimal stimuli preferentially recruit inhibitory interneurons (Blankenburg et al., 2003), which are known to be more sensitive to threshold-level vibratory stimuli (Andermann, Ritt, Neimark, & Moore, 2004; Swadlow, 2003; Mountcastle et al., 1969). Engagement of these neurons could decrease blood flow through a decrease in the net activity in a local volume of cortex (Shmuel, Augath, Oeltermann, & Logothetis, 2006) or through direct interactions between interneurons and the vasculature (Hamel, 2006; Cauli et al., 2004). Several alternative hypotheses exist for this dissociation, including the possibility that sensory-driven astrocytic activity is differently engaged by threshold-level somatosensory stimuli (Wang et al., 2006).

Poststimulus signal level in SI also failed to consistently correlate with hits versus misses. This finding is in agreement with recent studies showing that the mean firing rate in quickly adapting neurons in Areas 3b and 1 does not track detection (de Lafuente & Romo, 2005), if in disagreement with macroscopic-evoked response studies showing an association (Jones et al., 2007). These findings in SI present a divergence from fMRI studies in the visual system. Human V1 fMRI signal is correlated with psychophysical performance during detection of low-contrast stimuli (Ress, Backus, & Heeger, 2000). Furthermore,

V1 activity demonstrates a significant increase in activity during trials in which no change in stimulus is presented, ostensibly a function of increased attention during task performance (Ress et al., 2000; see also Ergenoglu et al., 2004). In contrast, evoked SI activity in this study was not consistently related to detection and did not show increases during task performance when a stimulus was not present. These divergent findings, obtained using the same basic technique (event-related fMRI) in the same species (human), suggest that primary visual and somatosensory cortex have substantially different rules for hemodynamic recruitment or that vision and somato-sensation employ different detection strategies in these representations.

Area SI Prestimulus Activity Predicts Detection Success

In contrast to the poststimulus signal, the prestimulus level of fMRI activity predicted perceptual performance, implicating SI dynamics in shaping the neural representations underlying detection. This finding is in good agreement with the demonstration that prestimulus oscillations in the SI hand representation predict perceptual success (Jones et al., 2010), particularly given the repeated observation that alpha oscillations negatively correlate with BOLD activity levels.

A variety of studies have shown that representations in primary somatosensory cortex are dynamically maintained, dependent on sensory context and ongoing state properties. In animal studies, neural adaptation to the pattern of ongoing stimulation transforms the spatial and temporal representation of subsequent tactile stimuli, with effects including decreasing the response to similar inputs, eliminating spikes that are not temporally associated with stimulus presentation (enhancing phase locking) and limiting the lateral spread of activation (Moore, 2004; Garabedian, Jones, Merzenich, Dale, & Moore, 2003; Kohn & Whitsel, 2002; Moore, Nelson, & Sur, 1999; Mountcastle & Powell, 1959). Similar paired-pulse suppression has been observed in the human (Hari & Forss, 1999; McLaughlin & Kelly, 1993). These neural transformations appear to correlate with perceptual competence. Stimulation 30 msec before a subsequent target stimulus can suppress the likelihood of detection, even when the priming stimulus is subliminal (Blankenburg et al., 2003).

Prestimulus state, characterized by the prevalence of activity in specific frequency bands, similarly predicts competence on many domains of behavioral performance (Lindsley, 1961). As referenced above, human MEG findings have shown that detection of threshold-level electrical stimuli applied to the finger is predicted by prestimulus power several frequency bands in SI (Jones et al., 2007; Linkenkaer-Hansen et al., 2004). Changes in state occurring on the microsecond timescale can also impact SI representations (Haslinger, Ulbert, Moore, Brown, & Devor, 2006; Sachdev, Ebner, & Wilson, 2004), suggest-

ing that more precise temporal measures of the ongoing pattern of SI activity will also predict perception.

Implications of These Findings for Neural Codes Supporting Detection

When the present findings are considered with previous studies, they suggest that SI plays a systematic role in detection. Changes in state measured with fMRI (this study) or MEG (Jones et al., 2010; Linkenkaer-Hansen et al., 2004) predict detection, as do differences in the SEP (Jones et al., 2007; Palva et al., 2005; Kullics, 1982). These lines of evidence are in contrast to the poststimulus fMRI signal (this study) and to action potential firing rate in the awake monkey (de Lafuente & Romo, 2005). Taken together, these findings suggest that the SI representation that is optimal for detection is characterized by differences in the temporal or spatial pattern of action potential activity and not the net "amount" (i.e., a rate code).

Differences in the temporal patterns of evoked activity for hits and misses could fail to register a correlated change in the fMRI signal in this study, as the hemodynamic changes measured by fMRI may be insensitive to changes in temporal pattern. Several lines of evidence support a frequency based code. In monkeys, Mountcastle and colleagues observed that in a class of Areas 3b and 1 neurons, whose firing properties resembled those of Meissner's afferents, the behavioral threshold for detection of a 30-Hz sinusoidal stimulus paralleled the lowest stimulus amplitude that evoked entrainment of firing (LaMotte & Mountcastle, 1975; Carli et al., 1971; see also Mountcastle et al., 1969). Similarly, studies in patients with implanted electrodes suggest that the detection of an electric shock is correlated with increased poststimulus gamma band coherence but not with changes in the amplitude of initial poststimulus evoked activity (Meador, Ray, Echauz, Loring, & Vachtsevanos, 2002). Human and animal recordings have also consistently observed a decrease in the prevalence of power in the 8–12 Hz alpha range in SI with sensory stimulation (Jones et al., 2010; Narici & Peresson, 1995; Lindsley, 1961). In addition to these frequency-specific SI patterns, Libet (2004) has proposed that temporal duration of SI activity, and not amplitude of activity, is the key signal required for the awareness of a tactile stimulus in humans. One general suggestion is that these temporal response properties may reflect the more efficacious communication between SI and other cortical regions. This prediction is supported by the finding that enhanced phase locking between sensori-motor regions and frontal and parietal cortices immediately following tactile stimulation correlates with the detection of an electrical stimulus (Palva et al., 2005; see also Bauer, Oostenveld, Peeters, & Fries, 2006).

A neural dynamic proposed to change downstream gain without necessarily changing firing rate locally is gamma band oscillatory activity. Synchronization of excitatory neuron firing is thought to increase firing rate in

efferent targets by providing optimal drive within crucial windows of opportunity (e.g., before the onset of feedforward inhibition; Knoblich, Siegle, Pritchett, & Moore, 2010; Moore, Carlen, Knoblich, & Cardin, 2010; Cardin et al., 2009). One scenario that fits all existing data, then, is that an ongoing dynamic such as gamma could coordinate spike timing in SI without increasing it. Such synchronization could explain enhanced macroscopic neurophysiological activity on hit trials (e.g., Jones et al., 2007) without increases in overall rate (de Lafuente & Romo, 2005): The preexistence of gamma or the conditions that promote its expression in the period immediately before the sensory stimulus could also be reflected in prestimulus fMRI signal, again consistent with known correlations between EEG and fMRI signals.

The spatial pattern of activation could also serve as a code that is independent of net fMRI activity level in the SI fingertip representation. The design of this study and our fMRI spatial resolution led us to analyze ROIs defined by maximal amplitude stimuli. In SI, the ROI likely corresponded to the full extent of the third digit distal finger pad representation. This analysis approach is insensitive to changes in the spatial pattern of activity within the ROI. Action potential recordings in SI can suffer from the converse problem, as they represent a point measurement, typically targeted to the center of a representation, and might similarly fail to observe a change in the spatial pattern of activation. As such, the spatial profile within the fingertip representation, but not the net activity level, could be a feature of signal transmission that leads to detection success. One kind of change in pattern could be the differential engagement of specific column types, a hypothesis supported by the existence of clusters of neurons in monkey SI with distinct adaptation properties (Sur, Wall, & Kaas, 1981). Ongoing dynamics could also modulate the spatial extent of SI activity. A broader extent of SI finger representation activation would be predicted to drive larger amplitude responses in spatially extensive SII/PV receptive fields and increased fMRI signal. In support of this hypothesis, the lateral extent of discrete somatosensory input can be actively modulated by SI cortical dynamics, and previous hypotheses suggest that broader activation profiles in SI are optimal for detection success (Moore, 2004; Moore et al., 1999).

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