Cerebral Cortex, 2021;00: 1–14

https://doi.org/10.1093/cercor/bhab301
Original Article

ORIGINAL ARTICLE

Neural Basis of Somatosensory Spatial and Temporal Discrimination in Humans: The Role of Sensory Detection

Cheng-Wei Huang[1], Chin-Hsien Lin[2], Yi-Hsuan Lin[3], Hsin-Yun Tsai[3] and Ming-Tsung Tseng[4]

[1]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan, [2]Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan, [3]Taiwan International Graduate Program in Interdisciplinary Neuroscience, National Taiwan University and Academia Sinica, Taipei, Taiwan and [4]Graduate Institute of Brain and Mind Sciences, National Taiwan University College of Medicine, Taipei, Taiwan

Address correspondence to Ming-Tsung Tseng, Graduate Institute of Brain and Mind Sciences, National Taiwan University College of Medicine, 1 Jen-Ai Road Section 1, Taipei 10051, Taiwan. Email: mingtsungtseng@ntu.edu.tw

Abstract

While detecting somatic stimuli from the external environment, an accurate determination of their spatial and temporal properties is essential for human behavior. Whether and how detection relates to human capacity for somatosensory spatial discrimination (SD) and temporal discrimination (TD) remains unclear. Here, participants underwent functional magnetic resonance imaging scanning when simply detecting vibrotactile stimuli of the leg, judging their location (SD), or deciding their number in time (TD). By conceptualizing tactile discrimination as consisting of detection and determination processes, we found that tactile detection elicited activation specifically involved in SD within the right inferior and superior parietal lobules, 2 regions previously implicated in the control of spatial attention. These 2 regions remained activated in the determination process, during which functional connectivity between these 2 regions predicted individual SD ability. In contrast, tactile detection produced little activation specifically related to TD. Participants' TD ability was implemented in brain regions implicated in coding temporal structures of somatic stimuli (primary somatosensory cortex) and time estimation (anterior cingulate, pre-supplementary motor area, and putamen). Together, our findings indicate a close link between somatosensory detection and SD (but not TD) at the neural level, which aids in explaining why we can promptly respond toward detected somatic stimuli.

Key words: functional magnetic resonance imaging, posterior parietal cortex, sensory detection, somatosensation, tactile discrimination

Introduction

While perceiving somatic stimuli from the external environment, the ability to accurately discriminate their spatial (i.e., spatial discrimination, SD) and temporal (i.e., temporal discrimination, TD) properties is essential for human behavior, but the underlying cerebral mechanisms remain unclear. In the human brain, the processing of somatosensory inputs has a hierarchical organization (de Haan and Dijkerman 2020), with sensory detection commonly assumed to be the initial process for higher-level spatial (Harris et al. 2004) and temporal (Yamamoto and Kitazawa 2016) assessments. Investigating how these assessments relate to sensory detection is thus pertinent to understanding the neural basis underlying somatosensory SD and TD. Surprisingly, little research has been done to address this issue.

At the behavioral level, there is evidence that the processing involved in somatosensory SD is closely related to its detection (Gallace and Spence 2008; Medina and Coslett 2016). Repetitive tactile stimulation has been demonstrated to enhance the processing of tactile spatial information (Godde et al. 2000). In addition, accurate localization of tactile stimuli has also been reported to depend on tactile detection (Harris et al. 2004; Harris et al. 2006) and require the information of skin location during tactile detection (Azanon et al. 2010; Brandes and Heed 2015). Together, these observations suggest that tactile detection may constitute a core process component for SD. Nevertheless, the neural underpinnings for the dependence of somatosensory SD on the detection process remain elusive. Interestingly, during tactile detection, a stimulus produces activation in topographically corresponding parietal regions, including the primary somatosensory cortex (SI) (Gelnar et al. 1998), secondary somatosensory cortex (SII) (Ruben et al. 2001), and posterior parietal cortex (Huang et al. 2012). This observation raises the possibility that the neural substrates predicting an individual's tactile spatial discriminability (i.e., SD ability) may already become activated during somatosensory detection.

With regard to the temporal aspect, the relationship between somatosensory detection and the processing underlying an individual's temporal discriminability (i.e., TD ability) remains elusive. Although current models propose that sensory detection provides the input for the neural network involved in higher-level temporal processing (de Haan and Dijkerman 2020), it has been demonstrated that impaired tactile TD was not accompanied by the failure to detect the presence of tactile stimuli (Hannula et al. 2008), suggesting that sensory detection itself might not be a major determinant for an individual's temporal discriminability. For somatosensory TD, a recent study has implicated SI in facilitating the discrimination of tactile temporal properties (Rocchi et al. 2016), but whether this could be attributed to the role of SI in sensory detection (rather than in processing the temporal information of somatic inputs) remains unclear. In terms of temporal information processing, compelling evidence points out that the cortico-basal ganglia circuitry is involved in the processing of temporal attributes in a variety of timing behaviors (Merchant et al. 2013), such as the timing of movements (Yin 2014), auditory stimuli (Rao et al. 2001; Teki et al. 2011), and visual events (Jin et al. 2009). It remains unclear whether this circuitry is also engaged in TD of somatic inputs.

In this work, we aimed to investigate whether and how sensory detection relates to individuals' behavior when they judge the spatial and temporal properties of tactile stimuli. In each trial, a pair of vibrotactile pulses was delivered from 1 of the 2 probes positioned on the proximal (designated as $Probe_{proximal}$) and distal (designated as $Probe_{distal}$) part of the left lower leg (Fig. 1A), and participants either judged the location of stimulation in an SD trial or decided whether the pulses were perceived as a single stimulus or 2 separate events in time in a TD trial (Pastor et al. 2004; Albanese et al. 2009). In another simple detection trial, participants were only asked to pay attention to the presence of stimulation but not requested to discriminate its spatial or temporal information. Given the conception that sensory detection provides the input for higher-level assessments (de Haan and Dijkerman 2020) implies that tactile SD and TD may consist of a detection component and a higher-level processing component, we propose that the neural mechanisms subserving SD (or TD) can be conceptualized as a dual process model, in which a detection process leads to tactile detection, and a determination process gives rise to accurate SD (or TD) behaviors (Harris et al. 2004; Takahashi et al. 2013; Miyazaki et al. 2016; Fig. 2). Assuming that tactile detection involved the neural substrates related to the processing of spatial properties of tactile stimuli, we hypothesized that these neural substrates might play a crucial role in determining an individual's spatial discriminability. If this is the case, we expected to find that responsivity and/or functional interaction within these neural substrates would reflect an individual's capacity for SD. As for TD, we did not hypothesize that tactile detection recruited the neural substrates specifically involved in temporal information processing to underlie an individual's tactile temporal discriminability. Instead, we posited that the somatosensory and cortico-striatal timing systems would subserve individual temporal discriminability during the determination process.

Materials and Methods

Participants

Forty-seven right-handed healthy adults took part in the current study as paid volunteers. Written informed consent was obtained from all participants before experiment. This study was approved by the Ethics Committee of National Taiwan University Hospital, Taipei, Taiwan. Seven participants were eliminated from analyses: 4 had abnormal findings from their structural brain magnetic resonance imaging (MRI), 2 failed to complete the entire experiment, and 1 had preprocessing errors. Consequently, data from 40 participants (24 females, age range: 20–78 years; mean $\pm$ SD: 53.5 $\pm$ 17.6 years) were analyzed.

Stimuli

An MR-compatible piezo-tactile stimulator system (Dancer Design, St. Helens, UK) with 2 stimulation probes containing a 2-channel amplifier and built-in oscillators was employed to deliver vibrotactile stimulation (Tseng et al. 2017). The 8-mm-diameter probe protrudes through a 10-mm-diameter hole to generate a tactile sensation (Fig. 1A). By using custom-written LabVIEW software (National Instruments, Austin, TX), we generated external voltage signal to control the amplitude of protrusion for each probe in this stimulator system. Because the probe is housed in a rectangular ceramic case, this system allows a shortest inter-probe distance (IPD) of 50 mm. Each vibrotactile pulse (10 ms duration) consisted of a half cycle of a sine wave at 50 Hz. Both cases were attached to the participant's left lower leg with Velcro straps without causing any discomfort. Presentation software (Neurobehavioral Systems, San Francisco, CA) was used for stimulus presentation and data acquisition.

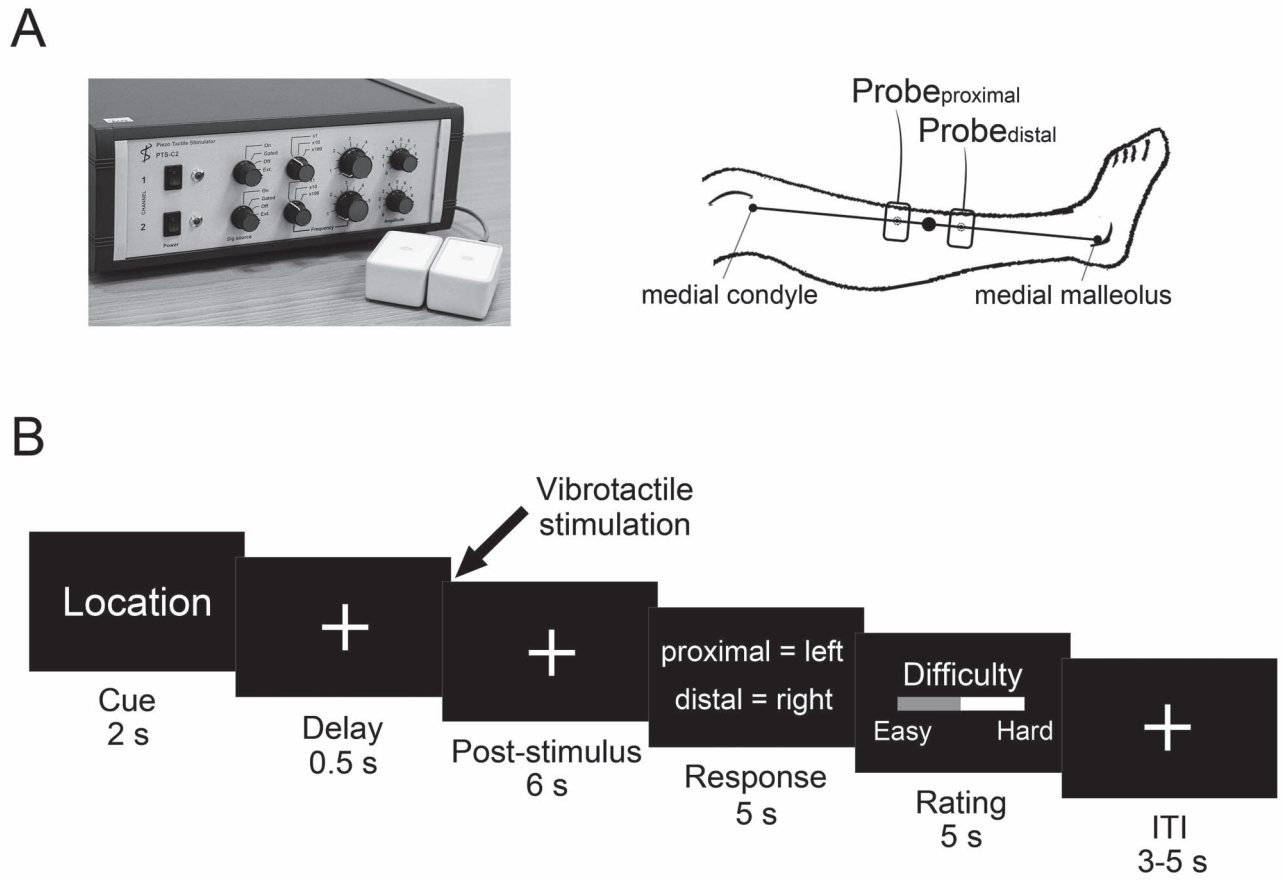

Figure 1. Vibrotactile stimulator and experimental paradigm. (*A*) During the behavioral and fMRI sessions, 2 probes were positioned on the line connecting the medial condyle and medial malleolus of the left leg. (*B*) An exemplary SD trial in which participants were required to discriminate stimulus location. A 2-s written cue denoted the trial type, which was followed by a 0.5-s delay period. A pair of vibrotactile pulses was then delivered from either the proximal ($Probe_{proximal}$) or distal ($Probe_{distal}$) probe. After a 6-s post-stimulus period, participants reported their decision by a button press as well as subjective task difficulty on a visual analogue scale. The intertrial interval was 3–5 s (jittered).

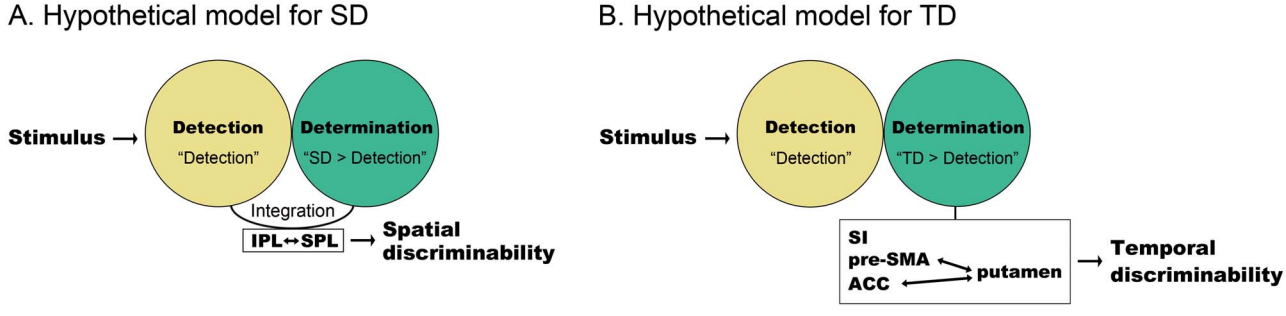

Figure 2. Hypothetical models and summary of fMRI results. (*A*) For tactile SD, we hypothesized that the neural substrates specifically involved in spatial information processing of somatic stimuli were activated during both detection (yellow) and determination (green) processes, which integrated relevant spatial information collected during both processes to underlie individual spatial discriminability. Our fMRI data demonstrated that the inferior (IPL) and superior (SPL) parietal lobules constituted these neural substrates, with the coupling between these 2 regions predicting individual SD ability. (*B*) Regarding tactile TD, we posited that tactile temporal discriminability was implemented in the neural substrates associated with the determination process (green). This speculation was confirmed in our fMRI data, which showed that responsivity within the primary somatosensory cortex (SI) and functional connectivities from the pre-SMA and ACC to the putamen covaried with individual TD ability. In (*A*) and (*B*), circles denote the process component, and rectangles indicate the involved neural substrates underlying spatial or temporal discriminability (double-headed arrows represent functional connectivity). fMRI contrasts used to identify the neural substrate underlying detection and determination processes are in double quotes.

Behavioral Session

Before the formal functional MRI (fMRI) session, participants took part in a behavioral session, during which 2 vibrotactile stimulation probes were positioned on the skin of the left leg (Fig. 1A). Individual tactile detection threshold (DT) was first assessed using the method of levels (see Supplementary Material for details; Yarnitsky 1997). We then assessed participants' tactile discrimination thresholds, including the IPD corresponding to an 80% correct response rate (designated as $IPD_{80\%CR}$) when they judged the location of stimulation, and the interstimulus interval (ISI) corresponding to an 80% correct response rate (designated as $ISI_{80\%CR}$) when they decided whether the pulses were perceived as a single stimulus or 2 separate events in time (Pastor et al. 2004; Albanese et al. 2009). To this end, we administered a series of testing blocks to determine $IPD_{80\%CR}$ during SD and $ISI_{80\%CR}$ during TD (see Supplementary Material for details). For each participant, the defined $IPD_{80\%CR}$ was used as the IPD between the 2 probes in the fMRI session of that participant. Note that, among our participants, 36 participants had an $IPD_{80\%CR}$ equal to or larger than 50 mm, and a 50 mm IPD produced a 100% correct response rate in 4 participants. For these 4 participants, their $IPD_{80\%CR}$, which might be overestimated, was determined as 50 mm. The $IPD_{80\%CR}$ value for all participants was 61.3 ± 9.5 mm (mean $\pm$ SD; range: 50–80 mm). In our pilot study, we observed that, with the stimulus parameters corresponding to 80% correct responses, task performance in TD trials tended to be lower than that in SD trials. In order to minimize the difference in task performance between both trial types, which may confound brain responses during tactile discrimination (Zhang et al. 2005; Adhikari et al. 2014), the $ISI_{80\%CR}$ in our participants (mean $\pm$ SD: 165.0 ± 103.3 ms; range: 40–495 ms) was used as the stimulus parameter for the TD trial in the fMRI session in 20 participants, and the parameter for the rest 20 participants was 3 times their $ISI_{80\%CR}$. Since the aim of the current study was to compare the role of sensory detection in SD with that in TD, and the age, gender, $IPD_{80\%CR}$, and $ISI_{80\%CR}$ values were not significantly different between these 2 groups (all $P > 0.4$), data from both groups were analyzed and reported together in the current study. Before the fMRI session, participants attended a practice session to minimize learning effects during scanning (see Supplementary Material for details).

fMRI Session

The fMRI session consisted of 2 scanning runs, with each run including 48 trials. There were 16 repetitions of each SD, TD, and simple detection trial in each run. The IPD and ISI determined in the behavioral session were used as the stimulus parameters in 14 trials of each trial type (i.e., the content of vibrotactile stimulation was identical in each of these 42 trials), and the fMRI analyses in the present study focused on these 42 trials. In each trial, a 2-s written cue indicated the trial type ("Location," "Number," and "Stimulus" for SD, TD, and simple detection trials, respectively), and 2 successive 10-ms vibrotactile pulses were delivered from a single probe ($Probe_{proximal}$ or $Probe_{distal}$) 0.5 s after the termination of the written cue (Fig. 1B). Given the current study focused on the role of sensory detection in tactile discrimination, participants were instructed to respond during the 5 s response period in each trial only when they detected the presence of vibrotactile stimulation after the 0.5-s delay period (Fig. 1B). In an SD trial, participants were required to decide whether the tactile stimulation was located at $Probe_{proximal}$ or $Probe_{distal}$. In a TD trial, participants had to decide whether they perceived a single stimulus or 2 temporally separate stimuli. For these 2 trial types, participants reported their decision by pressing, in less than 5 s, either the left (with the right index finger) or right (with the right middle finger) button of a response pad after a 6-s post-stimulus interval. For the response cue, the left and right buttons were randomly assigned to 1 of 2 locations ("proximal" or "distal") in SD trials and to 1 of 2 numbers ("1" or "2") in TD trials with equal frequency. At the end of each SD and TD trial, participants were asked to rate the task difficulty on a 0–100 visual analogue scale (anchored at left with "easy" and at right with "hard") within a time window of 5 s. In a simple detection trial, participants were instructed to pay attention to the detection of the vibrotactile pulses but were not requested to directly report the detection (Schroder et al. 2019). We used this design to minimize potential confounds arising from post-detection processes related to the reporting task during tactile detection (Tsuchiya et al. 2015; Cohen et al. 2020), which allowed us to examine whether the neural substrates responsible for the spatial and temporal processing of somatic stimuli were already activated during sensory detection. The response requested in a simple detection trial was simply to press 1 of the 2 buttons according to the displayed response cue (either "left" or "right"; presented randomly and with equal frequency), which, as mentioned above, signified that participants detected the presence of vibrotactile stimulation. To avoid confounding effects of motor preparation in all 3 trial types, participants were told not to respond until a response cue appeared. Trials were separated by an intertrial interval of 3–5 s (jitter). In the rest 6 trials (2 repetitions of each trial type), we used the same $IPD_{80\%CR}$ with a 5 ms ISI as the stimulus parameters. The behavioral data from these 6 trials were used as a validation check for the TD task in the current study (see Behavioral Results section). In the first-level general linear model (GLM) of our fMRI analysis (described below), these 6 trials were included in a separate regressor of no interest.

MRI Data Acquisition

A 3-Tesla Magnetom Prisma system equipped with a 64-channel head coil (Siemens, Erlangen, Germany) was used to acquire whole-brain fMRI data. Blood oxygen level-dependent (BOLD) responses were collected using a gradient-echo T2*-weighted echo-planar imaging (EPI) sequence (time repetition [TR] = 2000 ms; time echo [TE] = 30 ms; flip angle = 90°; field of view = 224×224 mm; a GRAPPA acceleration factor of 2; slice thickness = 3.9 mm; acquisition matrix = 64×64; voxel size = $3.5 \times 3.5 \times 3.9$ mm with 37 contiguous axial slices). The first 4 EPI volumes were discarded to allow the MR signal to reach steady state. To correct for inhomogeneity in the magnetic field (Hutton et al. 2002), field maps employing the same slice geometry as EPI images were collected using a double gradient-echo sequence (TR = 617 ms, $TE_1 = 10.00$, $TE_2 = 12.46$ ms). For registration purposes, a high-resolution T1-weighted magnetization-prepared rapid-acquisition gradient echo image (voxel size $0.88 \times 0.88 \times 0.89$ mm) and a structural T2-weighted scan coplanar with the functional images but with higher in-plane resolution (256×256) were also acquired.

fMRI Preprocessing

We used Statistical Parametric Mapping (SPM) 8 for image processing and analysis (Wellcome Department of Imaging Neuroscience, London, UK). All EPI volumes were unwarped using field

maps, realigned to the first image to correct for motion artifacts, and corrected for differences in slice acquisition timing. Subsequently, the resulting mean EPI image was co-registered with the T2-weighted structural image, which in turn was aligned with the T1-weighted image. The coregistered T1-weighted images were then segmented into gray matter, white matter, and cerebrospinal fluid according to the International Consortium for Brain Mapping East Asian brain template to create a study-specific template and individual flow fields using the Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra toolbox (Ashburner 2007). This registration tool has been demonstrated to be capable of eliminating registration difficulties related to the variation in brain structure among subjects with a large age range like ours (Peelle et al. 2012). The flow fields, which contained the deformation parameters to this study-specific template for each participant, were used to normalize each participant's realigned and resliced EPI volumes to the standard Montreal Neurological Institute (MNI) space (voxel size $2 \times 2 \times 2$ mm). Finally, data were spatially smoothed using a Gaussian kernel of full-width half-maximum 6 mm and temporally filtered to 1/128 Hz to remove low-frequency noise. In the current study, statistical parametric maps were overlaid on all participants' average T1-weighted images.

fMRI Analysis

After preprocessing, GLM was fitted to the fMRI data. Based on the events in each trial, the design matrix for the first-level analysis consisted of 17 regressors: $3 \times$ cue plus delay (2.5 s; 3 trial types), $4 \times$ post-stimulus (6 s; 3 trial types $+1$ regressor for missed trials and the 6 trials with a 5 ms ISI), $3 \times$ response (5 s; 3 trial types), $1 \times$ rating (5 s), and $6 \times$ motion parameters estimated during realignment. The intertrial interval was not modeled and served as the implicit baseline. The current study focused on the 3 post-stimulus regressors associated with the 3 trial types. In other words, across the 3 trial types, only trials with responses (i.e., trials in which participants detected tactile stimuli) were analyzed. To confirm whether fMRI results held in correctly responded trials, only trials with correct responses were modeled by these 3 post-stimulus regressors in a separate GLM, in which trials with incorrect responses were included in the regressor for missed trials and trials with a 5 ms ISI. All regressors were modeled as a boxcar function convolved with a canonical hemodynamic response function as implemented in SPM. These first-level individual t-contrasts were then fed to the second-level GLM analysis to determine significant voxels at the group level. Since age (Lenz et al. 2012; Brodoehl et al. 2013; Ramos et al. 2016) and gender (Sadato et al. 2000; Stephen et al. 2006) potentially confound brain activation related to tactile processing, both were included as covariates of no interest in all group-level contrasts in the current study. For all group-level regression analyses, we also regressed out the effect of subjective task difficulty, which would modulate brain activation related to tactile decision-making (Pleger et al. 2006).

To denote different process components during SD and TD, we use the term "detection process" for the process underlying an individual's tactile detection and "determination process" when referring to the process that was additional to the detection process during SD and TD in the current study. In other words, SD and TD are conceptualized as consisting of a detection process component and a determination process component (Fig. 2). Since participants were not asked to perform any discrimination during a simple detection trial, its associated brain activation (i.e., contrast "Detection"; brain activation during simple detection trials contrasted against baseline) was used to represent the neural response underlying the detection process in SD and TD trials (Fig. 2), and the neural substrates associated with the determination process during SD and TD were identified by the contrasts "SD > Detection" (Fig. 2A) and "TD > Detection" (Fig. 2B), respectively. A conjunction analysis between contrasts "SD > Detection" and "TD > Detection" was carried out to check whether the common neural substrates involved during the determination process of SD and TD were similar to previous research (Pastor et al. 2004). To clarify whether the neural substrates specifically involved in processing the spatial properties of somatic stimuli were already activated during the detection process, we also examined the brain structures whose activities were specifically enhanced during SD (i.e., contrast "SD > TD") or TD (i.e., contrast "TD > SD") and then conducted conjunction analyses between these specific contrasts and the contrast "Detection." We first performed whole-brain analyses on all the above-mentioned contrasts and then conducted conjunction analyses to elucidate the relationship between detection- and determination-related neural responses.

Because our data did not suggest a vital role of the detection process in determining participants' tactile temporal discriminability, we additionally performed a small-volume correction (SVC) analysis in the contralateral SI leg area for TD, based on the hypothesis that this region may contribute to the judgment of tactile temporal information (Conte et al. 2012; Rai et al. 2012; Rocchi et al. 2016). Given that Brodmann area 3b is the main center to receive inputs from the ventroposterior thalamic nucleus for tactile processing (Keysers et al. 2010), responds selectively to the stimulation of specific skin areas (Ann Stringer et al. 2014; Martuzzi et al. 2014), and has been implicated in encoding the temporal information of tactile stimuli from primate studies (Romo et al. 1998; Romo and Salinas 2003; Romo and de Lafuente 2013), the SVC analysis of the right SI focused on this cytoarchitectonic area. Considering the existence of somatotopic organization, this SI region of interest (ROI) was defined as a box centered at MNI coordinates $x/y/z = 12.7/-38.1/66.0$ and, respectively, extended ± 2.2, ± 2.0, and ± 2.9 mm along the x-, y-, and z-axes, as in a prior fMRI study applying tactile stimuli to the left calf (Akselrod et al. 2017).

Psychophysiological Interaction Analysis

Psychophysiological interaction (PPI) identifies voxels whose time course covaries differentially with that in a seed region as a function of different experimental conditions (Friston et al. 1997). To test whether participants' SD performance was implemented in the neural substrates that were specifically involved in processing the spatial properties of somatic stimuli during the detection process, a PPI analysis seeded at the right inferior parietal lobule (IPL), which has been implicated in tactile target detection (Goltz et al. 2015), was conducted using the generalized PPI toolbox in SPM (http://www.nitrc.org/projects/gppi; McLaren et al. 2012). Because we hypothesized that tactile detection activated the neural substrates responsible for spatial information processing to underlie individual spatial discriminability (Fig. 2A), the IPL seed was defined as the intersection between the IPL mask in the automated anatomical labeling (AAL) ROI library (Tzourio-Mazoyer et al. 2002) and the conjointly activated regions found by the conjunction analysis of group-level contrasts "SD > TD" and "Detection" (whole-brain

correction). We then performed an SVC analysis in an inter-subject regression analysis using individual SD performance as a covariate during the determination process (i.e., contrast "SD > Detection") in the right superior parietal lobule (SPL)—a key structure linked to spatial attentional shift (Molenberghs et al. 2007; Caspari et al. 2018) that has been implicated in localizing sensory stimuli (Bushara et al. 1999; Vandenberghe et al. 2001; Malhotra et al. 2009)—whose ROI mask was defined as the intersection between the SPL mask in the AAL ROI library and the conjointly activated regions revealed by the conjunction analysis of group-level contrasts "SD > TD" and "Detection."

As for TD, we ran 2 separate PPI analyses with anterior cingulate cortex (ACC) and pre-supplementary motor area (pre-SMA) as seed, because these 2 regions have been implicated in discriminating temporal attributes of tactile stimuli (Pastor et al. 2004). We performed SVCs in the right putamen—a critical subcortical region associated with time estimation (Coull et al. 2004; Merchant et al. 2013)—in an inter-subject regression analysis using individual TD performance as a covariate during the determination process (i.e., contrast "TD > Detection"). Because we hypothesized that the neural process underlying temporal discriminability was implemented in the determination process (Fig. 2B), the ACC seed was defined as the intersection between the ACC mask in the AAL ROI library and the activated regions during the determination process in TD trials (group-level contrast "TD > Detection"; whole-brain correction). Based on previous research investigating the parcellation of the medial frontal cortex (Kim et al. 2010; Zhang et al. 2012), the pre-SMA seed was defined as the anterior portion (i.e., $y \geq 0$) of the intersection between the SMA mask in the AAL ROI library and the activation during the determination process in TD trials (group-level contrast "TD > Detection"; whole-brain correction). The ROI mask of the right putamen was acquired from the AAL atlas. For all PPI analyses, we first extracted each participant's deconvolved time courses from the entire seed region defined above to generate the physiological regressor. Subsequently, the extracted time courses were multiplied with the different experimental conditions (i.e., SD, TD, and simple detection trials) to constitute the PPI term. Individual PPI maps were then entered into a second-level random-effects group analysis.

For group-level inference in our fMRI data, we used non-parametric cluster-wise permutation tests (SnPM13; http://warwick.ac.uk/snpm; Nichols and Holmes 2002) to control for false positives due to multiple testing (Eklund et al. 2016). Estimations were based on 5000 permutations without variance smoothing. Results were considered significant based on a threshold of $P < 0.05$ with family-wise error (FWE) correction. For SVC analyses within our defined ROIs, we used a voxel-wise threshold of $P < 0.05$ (FWE corrected) to correct for multiple testing.

Statistical Analysis

Statistical tests were performed with SPSS (Chicago, IL) and GraphPad Prism (GraphPad Software, San Diego, CA). One-sample *t* tests were conducted to check whether the correct rate of task performance during scanning was significantly above chance. Paired *t* tests were employed to compare the response rate, task performance, and difficulty level between SD and TD trials. Pearson's correlation test was used to examine the relationship between participants' detection and discrimination thresholds.

Results

Behavioral Results

In our fMRI paradigm, participants were instructed to respond in each trial only when they detected the presence of vibrotactile stimulation. Overall, participants made responses during the response period (Fig. 1B) in most trials (mean response rate ≥97.5% across the 3 trial types), indicating that participants were capable of detecting most tactile stimuli. For the task performance during the fMRI session, the rate of correct responses was significantly above chance (i.e., 50%) in both SD trials (mean ± SD: 79.8 ± 13.4%; $P < 0.0001$) and TD trials (74.6 ± 16.7%; $P < 0.0001$). When participants temporally discriminated 2 afferent tactile stimuli, the rate of correct responses in TD trials, in which the ISI was at least 40 ms in our participants, was also significantly higher than that in trials with a 5 ms ISI (7.5 ± 17.2%; $P < 0.0001$). These findings confirm that participants correctly performed both types of discrimination tasks. Importantly, the response rate (SD trials: 97.5 ± 4.5; TD trials: 98.6 ± 3.2%; $P = 0.069$), correct rate ($P = 0.065$), and subjective task difficulty (SD trials: 45.3 ± 20.7; TD trials: 43.4 ± 19.0; $P = 0.168$) were not significantly different between SD and TD trials, which allows us to compare their brain responses without being hampered by the confound of behavioral differences between both types of task (Binder et al. 2004; Zhang et al. 2005; Pleger et al. 2006; Adhikari et al. 2014).

Across individuals, participants' DT and $IPD_{80\%CR}$, but not $ISI_{80\%CR}$, increased monotonically with age (DT: $r = 0.452$, $P = 0.004$; $IPD_{80\%CR}$: $r = 0.363$, $P = 0.021$; $ISI_{80\%CR}$: $r = -0.116$, $P = 0.475$). Participants' tactile DT showed a significant positive correlation with their $IPD_{80\%CR}$ ($r = 0.478$, $P = 0.002$; Fig. 3A) but was not significantly associated with their $ISI_{80\%CR}$ ($r = 0.029$, $P = 0.860$; Fig. 3B). The correlation between $IPD_{80\%CR}$ and $ISI_{80\%CR}$ did not reach statistical significance ($r = -0.204$, $P = 0.207$; Fig. 3C). These results held when we excluded the 4 participants whose $IPD_{80\%CR}$ might be overestimated. Together, these findings suggest that tactile SD was closely linked to sensory detection.

Activation Related to Detection Process and Determination Process

The detection of a tactile stimulus (contrast "Detection") entailed significant BOLD activation in broadly distributed brain areas, such as the somatosensory (SII), prefrontal (including the insula and cingulate), motor-related, posterior parietal (including the IPL and SPL), temporal, and occipital regions (Supplementary Table S1). Most activations were observed bilaterally. The contralateral SI leg area was not significantly activated ($P = 0.337$). Consistent with previous tactile discrimination research (Pastor et al. 2004), a conjunction analysis between the determination process in SD (i.e., contrast "SD > Detection") and TD (i.e., contrast "TD > Detection") trials produced common activations in a wide variety of cortical (somatosensory, frontal, and posterior parietal cortices) and subcortical (thalamus, caudate, and cerebellum) regions (Supplementary Tables S1 and S2). Compared with TD, SD (contrast "SD > TD") was specifically associated with increased responsivity in the right hemisphere, including the SI, superior and middle frontal gyri, precentral area, IPL, SPL, angular gyrus, supramarginal gyrus, precuneus, and visual cortex (Table 1 and Supplementary Table S1). By contrast, the determination process in TD relative to SD (contrast "TD > SD") specifically entailed increased activation within 1) the bilateral cingulate cortex (including the ACC),

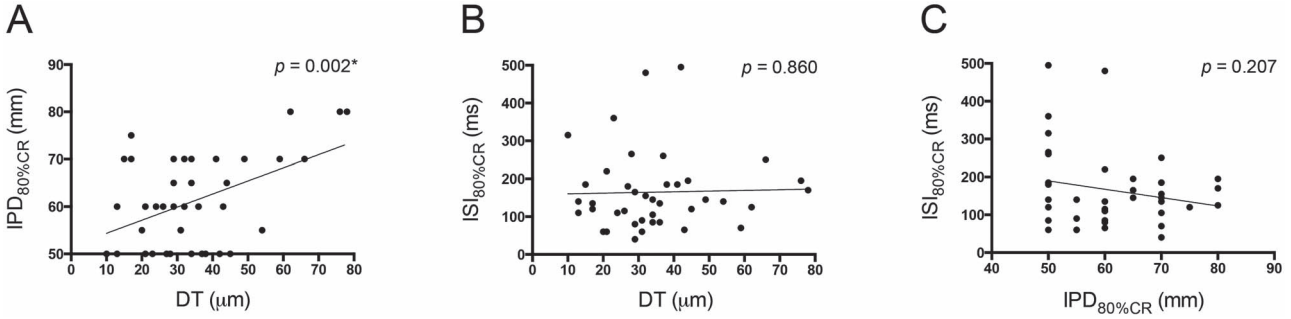

Figure 3. Between-subject correlations between tactile detection and discrimination thresholds. (*A*) Tactile DT was positively correlated with the IPD corresponding to an 80% correct response rate ($IPD_{80\%CR}$) during SD ($P = 0.002$). (*B*) No significant relationship was found between DT and the ISI corresponding to an 80% correct response rate ($ISI_{80\%CR}$) during TD ($P = 0.860$). (*C*) There was no significant correlation between the $IPD_{80\%CR}$ during SD and the $ISI_{80\%CR}$ during temporal discrimination ($P = 0.207$). $^*P < 0.05$.

superior and middle frontal regions, IPL, and angular gyrus; 2) the right pre-SMA; and 3) the left inferior frontal gyrus, SMA, precuneus, and middle temporal lobule (Table 1 and Supplementary Table S1).

Neural Substrates of Tactile Spatial Discriminability

Based on the assumption that SD consisted of a detection process component and a determination process component (Fig. 2*A*), and our behavioral data suggest a close relationship between SD and sensory detection, it is plausible to assume that detection-associated neural substrates might have a crucial role in determining an individual's tactile spatial discriminability. Interestingly, previous functional imaging studies have revealed that tactile detection activates parietal regions in a somatotopic manner (Hlushchuk and Hari 2006; Huang et al. 2012; Schafer et al. 2012), suggesting the possibility that tactile detection inherently activates the neural substrates that are specifically related to the processing of spatial properties of somatic stimuli (Gallace and Spence 2008; Medina and Coslett 2016). On the behavioral level, previous research has also demonstrated that both the detection process and further process related to stimulus localization were required for successful localization of tactile stimuli (Harris et al. 2004). Based on these observations, a parsimonious model regarding tactile SD is that brain structures that are specifically related to spatial information processing of somatic stimuli are activated not only during the detection process but also during the determination process, so as to integrate relevant spatial information collected during both processes to underlie a participant's tactile spatial discriminability (Fig. 2*A*).

To examine whether tactile detection activated the neural substrates specifically involved in processing the spatial properties of somatic stimuli, we carried out a conjunction analysis between "Detection" (whole-brain correction) and "SD > TD" (whole-brain correction) contrasts. This conjunction analysis, which allowed us to examine whether brain structures whose activities were specifically enhanced during SD were already activated during tactile detection, identified significant activation in the right frontoparietal areas, including the superior and middle frontal regions, precentral area, IPL, SPL, angular gyrus, supramarginal gyrus, and precuneus (Fig. 4*A*; Table 1 and Supplementary Table S1). Among these regions, only the right posterior parietal regions encompassing the IPL and SPL remained activated when only correct trials were included in this conjunction analysis (Supplementary Fig. S1). Here activation within these 2 regions was also noted during the determination process (i.e., contrast "SD > Detection"; Supplementary Table S1). These results suggest that the neural substrates that were specifically related to the processing of spatial properties of somatic stimuli were activated during both detection and determination processes.

Given that previous research suggests a close link between tactile detection and stimulus localization (Harris et al. 2004), and evidence indicates that the parietal attentional system plays an important role in localizing sensory stimuli (Bushara et al. 1999; Vandenberghe et al. 2001; Malhotra et al. 2009), we further hypothesized that, within the identified posterior parietal region in the right hemisphere, the IPL—a region implicated in tactile target detection (Goltz et al. 2015)—might interact with the SPL—a region associated with the allocation of spatial attention (Molenberghs et al. 2007)—during SD to underlie a participant's spatial discriminability. Importantly, in a group-level regression analysis using individual task performance in SD trials as a covariate, the functional connectivity between the right IPL and right SPL covaried with the task performance in SD trials during the determination process (i.e., contrast "SD > Detection") [peak MNI coordinates for the first suprathreshold cluster x/y/z = 22/−58/62, $t_{(1,35)} = 3.50$, $P = 0.041$; for the second suprathreshold cluster 16/−68/58, $t_{(1,35)} = 3.48$, $P = 0.043$; SVC, FWE-corrected; Fig. 4*B*] but not during the detection process (i.e., contrast "Detection"; $P = 0.652$).

Neural Substrates of Tactile Temporal Discriminability

To examine whether tactile detection also activated brain regions specifically involved in processing the temporal properties of tactile stimuli, we conducted another conjunction analysis between "Detection" (whole-brain correction) and "TD > SD" (whole-brain correction) contrasts. Strikingly, this analysis revealed barely overlapping activation over the entire brain (only 3 voxels in the pre-SMA). When only correct trials were analyzed, this conjunction analysis revealed no overlapping voxels (Supplementary Fig. S1). Because these findings did not support the idea that interpretation of tactile temporal information was already initiated during the detection process, which was indeed in line with our behavioral finding that participants' DT was unrelated to their $ISI_{80\%CR}$ (Fig. 3*B*), we therefore speculated that perhaps the neural process underlying tactile temporal discriminability was implemented in the determination process

Table 1 Brain activation specific to SD and TD

		SD > TD		TD > SD	
Area	Side	x/y/z (t)	Cluster no.	x/y/z (t)	Cluster no.
SI	R	28/−42/46 (3.58)	1 (599)*	–	–
ACC	R	–	–	6/46/14 (4.35)	1 (2372)
	L	–	–	−2/48/16 (4.78)	1
MCC	R	–	–	2/−24/40 (6.50)	2 (672)
	L	–	–	−2/−18/46 (3.95)	2
PCC	R	–	–	8/−42/30 (3.79)	2
	L	–	–	0/−40/30 (4.16)	2
SFG	R	28/2/54 (4.65)	2 (373)*	14/52/38 (7.37)	1
	L	–	–	−18/56/30 (6.70)	1
mSFG	R	–	–	4/56/20 (5.34)	1
	L	–	–	−8/52/40 (6.17)	1
MFG	R	30/2/54 (4.66)	2*	20/58/26 (5.48)	1
	L	–	–	−40/26/46 (5.05)	1
				−34/42/−12 (5.60)	3 (134)
IFG	L	–	–	−42/34/−10 (5.22)	3
PCA	R	32/0/50 (3.91)	2*	–	–
SMA	L	–	–	−2/−18/48 (3.88)	2
Pre-SMA	R	–	–	10/22/62 (3.95)	1
IPL	R	36/−46/54 (4.47)	1*	54/−56/44 (5.18)	4 (207)
	L	–	–	−54/−52/46 (3.69)	5 (462)
SPL	R	38/−46/56 (4.59)	1*	–	–
AG	R	40/−64/24 (4.53)	3 (166)*	50/−60/50 (4.80)	4
	L	–	–	−54/−60/38 (5.77)	5
SMG	R	34/−40/46 (3.63)	1*	–	–
Precuneus	R	12/−60/58 (3.99)	1*	–	–
	L	–	–	−4/−50/38 (5.14)	2
MTL	L	–	–	−62/−18/−8 (4.56)	6 (351)
VC	R	42/−74/32 (4.78)	3*	–	–

This table shows peak coordinates, *t* value, and activated cluster size (in voxels in parentheses) of activated brain regions of whole-brain analyses using SnPM (FWE correction at a cluster-level of $P < 0.05$) during the 6-s post-stimulus period. Activated clusters are numbered (e.g., contrast "SD > TD" produced 3 activated clusters, whose sizes were 599, 373, and 166 voxels), and activation foci corresponding to different anatomical locations within the clusters are given as MNI coordinates (in millimeters). *Overlapping clusters between contrasts "SD > TD" and "Detection". AG, angular gyrus; IFG, inferior frontal gyrus; L, left; MCC, middle cingulate cortex; MFG, middle frontal gyrus; mSFG, medial superior frontal gyrus; MTL, middle temporal lobule; PCA, precentral area; PCC, posterior cingulate gyrus; R, right; SFG, superior frontal gyrus; SI, primary somatosensory cortex; SMG, supramarginal gyrus; VC, visual cortex.

(Fig. 2*B*). To test this conjecture, we conducted the following group-level regression analyses in SPM.

First, previous studies have suggested that SI might reduce input noise to facilitate the discrimination of tactile temporal properties (Rocchi et al. 2016). We thus regressed brain activation associated with TD trials on participants' TD task performance and found that, although the correlation between SI responsivity and the TD performance was not significant during the entire TD process (i.e., brain activation during TD trials contrasted against baseline; $P = 0.503$; SVC, FWE-corrected), this correlation was significant during the determination process (i.e., "TD > Detection"; peak MNI coordinates $x/y/z = 14/-40/64$, $t_{(1,35)} = 2.27$, $P = 0.042$; SVC, FWE-corrected; Fig. 5*A*).

Second, in light of the growing literature indicating a critical role of the cortico-basal ganglia circuitry in temporal information processing (Coull et al. 2004; Merchant et al. 2013), we hypothesized that the cortical regions associated with the determination process would interact with the subcortical structures involved in time estimation, particularly the putamen, to subserve tactile temporal discriminability. To test this hypothesis, we conducted 2 separate PPI analyses using the ACC and pre-SMA as seed, because both regions were activated during the determination process in TD trials ("TD > Detection" in Supplementary Table S1) and have been implicated in discriminating temporal attributes of tactile stimuli (Pastor et al. 2004). Importantly, we found that the coupling from both the ACC and pre-SMA to the dorsal part of the right putamen was positively correlated with participants' TD performance (ACC-putamen coupling: peak MNI coordinates $x/y/z = 28/-10/10$, $t_{(1,35)} = 3.95$, $P = 0.049$; pre-SMA-putamen coupling: peak MNI coordinates $x/y/z = 28/-10/14$, $t_{(1,35)} = 4.38$, $P = 0.019$; SVC, FWE-corrected; Fig. 5*B*). Notably, the strength of these 2 functional connectivities was also significantly correlated with each other ($r = 0.536$, $P = 0.0004$; Fig. 5*C*).

Discussion

The current study aimed at investigating the neural mechanism underlying the relationship between somatosensory detection and spatial and temporal discrimination. By controlling for the response rate, task performance, and task difficulty between SD and TD tasks, we demonstrated that, although the determination process of SD and TD involved common brain regions, the role of sensory detection appeared to be different between both types of tactile discrimination. The neural substrates specifically involved in processing the spatial properties of somatic stimuli (i.e., IPL and SPL) were already activated during the

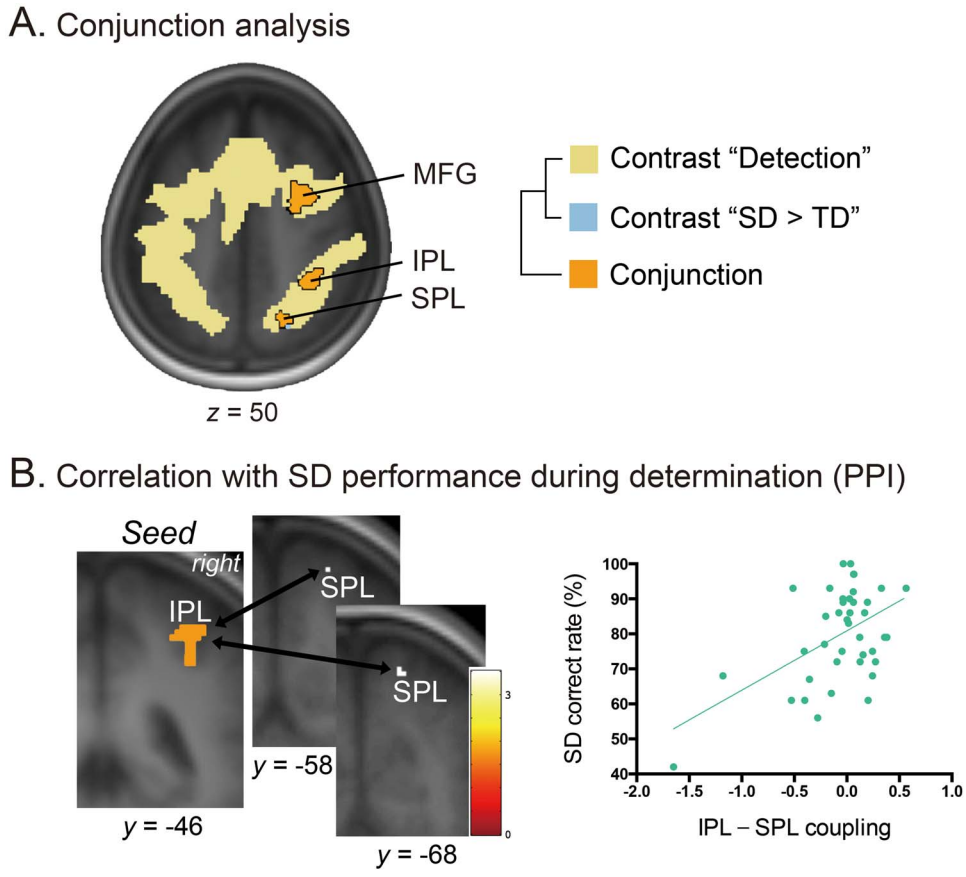

Figure 4. Neural mechanisms underlying tactile spatial discriminability. (*A*) A conjunction analysis between brain activations during tactile detection (contrast "Detection"; yellow) and those specifically enhanced during SD (contrast "SD > TD"; blue). The overlap in activation, which included the middle frontal gyrus (MFG), IPL, and SPL, is shown in orange. For each contrast, activated clusters survived correction for multiple comparisons at the whole-brain level and are rendered on all participants' average T1-weighted images. (*B*) In a PPI analysis, the strength of the coupling from the IPL (seed) to the SPL during the determination process (i.e., contrast "SD > Detection"; green) predicted a participant's spatial discriminability (note that this SVC analyses produced 2 suprathreshold clusters). The strength of coupling in the scatter plot is extracted from the suprathreshold cluster. In (*B*), the color bars represent the *t* scores of the group analysis in SPM. Activation clusters displayed here survived SVCs ($P < 0.05$, FWE corrected) and were rendered on all participants' average T1-weighted images.

detection process and predicted participants' spatial discriminability during the determination process, which mirrored the linear relationship between participants' sensitivity to perceive tactile stimuli (i.e., DT) and to discriminate spatial information (i.e., $IPD_{80\%CR}$). By contrast, tactile detection entailed little activation specifically engaged in processing the temporal properties of somatic stimuli, which paralleled the lack of relationship between participants' sensitivity to perceive tactile stimuli and to discriminate temporal information (i.e., $ISI_{80\%CR}$). Participants' temporal discriminability was subserved by the somatosensory cortex and cortico-striatal circuitry during the determination process.

Consistent with previous neuroimaging research (Hlushchuk and Hari 2006; Albanese et al. 2009; Brodoehl et al. 2013; Grund et al. 2021), tactile stimulation in our simple detection trial led to activation in many frontal, parietal, and temporal regions. Among these regions, the SII, insula, cingulate, motor regions, and superior temporal cortex have been implicated in different processes during tactile detection (Moore et al. 2013; Schroder et al. 2019). The absence of activation in the contralateral SI leg area might be explained by the engagement of low cognitive demands during simple detection relative to higher-order discriminative tasks (Albanese et al. 2009). Importantly, we showed that tactile detection activated brain structures whose activities were specifically enhanced during spatial (but not temporal) discrimination. Because the trial number was identical for SD and TD trials in our paradigm, and the response rate, task performance, and difficulty level were comparable between these 2 trial types, this phenomenon could not be attributed to the difference in our paradigm between SD and TD trials. Our findings thus demonstrate that tactile detection activates the neural system underlying SD, suggesting that humans simultaneously process spatial features when they encounter somatic stimuli.

It is a matter of debate whether somatosensory SD and detection are 2 mutually dependent or independent processes. Some evidence from studies on healthy human adults points toward the dependence of SD on detection (Harris et al. 2004), while investigations on brain-damaged individuals suggest that both processes seem to be dissociable (Paillard et al. 1983; Halligan et al. 1995; Rossetti et al. 1995; Rapp et al. 2002). In the present study, we demonstrated that tactile SD was closely linked to tactile detection. Behaviorally, we found that participants' DT predicted their $IPD_{80\%CR}$. At the neural level, we revealed that the right IPL and SPL, whose responsivity was specific to SD, remained activated during both detection and determination

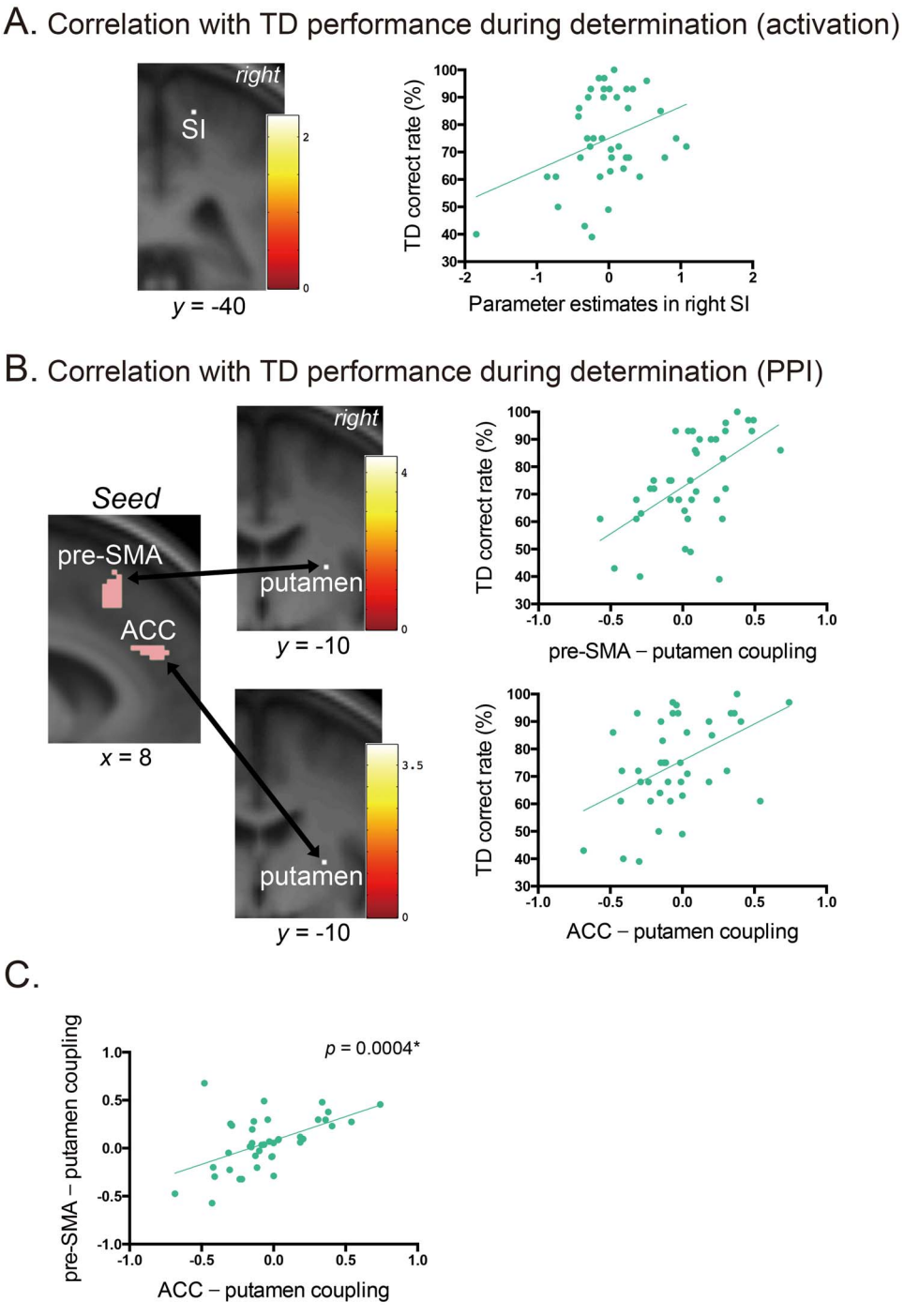

Figure 5. Neural mechanisms underlying tactile temporal discriminability. (*A*) Responsivity in the right primary somatosensory cortex (SI) scaled with individual TD performance during the determination process (i.e., contrast "TD > Detection"; green). (*B*) In 2 separate PPI analyses using the pre-SMA and ACC as seed, the strength of functional coupling from the seed region to the right putamen increased as a linear function of participants' TD performance during the determination process (i.e., contrast "TD > Detection"; green). The color bars represent the *t* scores of the group analysis in SPM. Activation clusters displayed here survived SVCs ($P < 0.05$, FWE corrected) and are rendered on all participants' average T1-weighted images. The strength of functional coupling in the scatter plots is extracted from the suprathreshold cluster. (*C*) Functional connectivities from the ACC and pre-SMA to the right putamen in (*B*) covaried with each other ($P = 0.0004$) during the determination process (contrast "TD > Detection").

processes and determined participants' SD performance during the determination process. Since activation within these 2 regions is part of the detection process and determines SD performance, it is plausible that lesions involving these 2 regions would impair both detection and SD, whereas those involving brain structures which only respond during the detection or determination process would mainly affect detection or SD, respectively. Our findings thus provide a neural account which may reconcile the disparate findings from healthy and brain-damaged subjects.

The finding that tactile detection already entailed IPL and SPL activations supports the notion that brain responses elicited by sensory detection foster spatial information processing of somatic inputs. Having said that, the persistent activation of the IPL and SPL during both the detection and determination processes, as well as the prediction of IPL–SPL coupling for SD performance during the determination (but not detection) process, suggests that, in additional to the detection process, this parietal network requires further process to integrate relevant spatial information acquired during both processes to correctly determine stimulus location. In the context of spatial cognition, the posterior parietal cortex has been construed as a key region for spatial information processing of sensory events, including the visual (Kravitz et al. 2011) and auditory (van der Heijden et al. 2019) stimuli. In the tactile domain, the right posterior parietal cortex has also been assumed to represent and integrate spatial information relevant for localization (Reed et al. 2005; Azanon et al. 2010). In our SD task, the engagement of the posterior parietal cortex on the right hemisphere basically converges on these notions. In terms of attention, the IPL, which has been implicated in sustained tactile attention (Goltz et al. 2015) and spatial attention (Thiebaut de Schotten et al. 2005), has been conceptualized as a center for stimulus-driven attentional control (Corbetta and Shulman 2002). In contrast to IPL, the SPL is mainly involved in voluntary shifts of spatial attention (Corbetta and Shulman 2002; Molenberghs et al. 2007; Caspari et al. 2018), including the deployment of spatial attention to visual (Corbetta et al. 2000), auditory (Bushara et al. 1999), and tactile (Burton et al. 1999) events. These observations, in conjunction with above-described persistent IPL and SPL activation during the entire SD process as well as prediction of IPL-SPL connectivity for SD performance, lead us to propose that an accurate assessment of somatosensory spatial properties arises from the dynamic interaction between top-down and bottom-up control of spatial attention in the posterior parietal cortex. Given we did not find a role of the SI and SII, whose activities also reflect spatial features during somatic detection (Gelnar et al. 1998; Ruben et al. 2001), our proposed mechanism supports the concept that the assessment of somatosensory spatial properties requires higher-order cognitive processes (i.e., the determination process in the current study), rather than simple somatotopic representation in the somatosensory cortex (Medina and Coslett 2016; Azanon and Longo 2019).

In contrast to SD, our findings did not support a key role of tactile detection in determining an individual's temporal discriminability, because participants' DT did not parallel their $ISI_{80\%CR}$, and we found no evidence to indicate the presence of brain responses specifically engaged in processing tactile temporal information during tactile detection. During the determination process, we revealed that SI activation reflected individual TD performance. Although the contribution of SI to tactile TD has been reported previously (Conte et al. 2012; Rai et al. 2012; Rocchi et al. 2016), it remains unclear whether this contribution emanates purely from its role in sensory detection (Hlushchuk and Hari 2006; Jones et al. 2007; Schafer et al. 2012), or in other neural processes needed for TD, such as working memory (Harris et al. 2002) and noise reduction (Rocchi et al. 2016). Here, we found no significant SI activation during tactile detection, and SI activity predicted TD performance during the determination process, but not during the entire TD process. These findings argue that SI is indeed endowed with a mechanism to process the temporal information of somatic inputs. This interpretation is supported by the role of SI in tactile discrimination as revealed from primate studies, in which quickly adapting SI neurons encode the temporal structure of tactile stimuli and modulate their firing rates according to the encoded temporal information to facilitate perceptual judgments (Hernandez et al. 2000; Luna et al. 2005).

Along with SI, our data also showed that the coupling from the ACC and pre-SMA to the putamen predicted individual TD performance during the determination process, which is consistent with previous studies reporting the involvement of ACC, pre-SMA (Pastor et al. 2004), and putamen (Lyoo et al. 2012) in TD. Given that neurons within these 3 regions have been demonstrated to code for time intervals (Matell et al. 2003; Mita et al. 2009; Kim et al. 2013), this result endorses the notion that ensembles of cortical and striatal neurons encode temporal information (Matell and Meck 2004), extending the existing knowledge about the role of the cortico-striatal circuitry in temporal information processing into the somatosensory domain. The finding that pre-SMA was related to tactile temporal discriminability during the determination process supports its role in the transformation from representing somatosensory inputs to generating a discrimination decision (Hernandez et al. 2002). Regarding the ACC, the firing pattern of neurons within this region has been demonstrated to be modulated by time intervals after the to-be-estimated interval is terminated, suggesting its involvement in the decision-making process associated with time estimations (Matell et al. 2003; Kim et al. 2013). Importantly, the identified functional connectivities of pre-SMA and ACC not only converged in the dorsal putamen but also correlated with each other. This finding is in good accordance with the striatal beat-frequency model of interval timing, in which the medium spiny neurons in the dorsal striatum integrate temporal patterns of simultaneous neuronal activity in different cortical regions (Merchant et al. 2013). Considering that area 3b—the SI subregion we examined—appears to code the temporal structure of sensory stimuli (Murray et al. 2014; Rossi-Pool et al. 2021), and primate studies suggest that SI drives higher cortical regions to generate perceptual reports (Romo and de Lafuente 2013), we posit that quickly adapting neurons within SI may integrate relevant temporal information into a temporal code and then distribute this code to the cortico-striatal timing system to reach a decision report.

In conclusion, the current study elucidates the neural mechanisms underlying the link between somatosensory detection and SD—which arises from the integration of spatial information in parietal attentional systems during both detection and determination processes—but not TD—which relies on temporal information processing in the somatosensory cortex and generation of perceptual reports in cortico-striatal timing systems during the determination process. The revealed neural basis underlying the close relationship between somatosensory detection and SD—which is already present at the early stage of human development (Bremner et al. 2008)—not only elucidates the substantial influence of somatosensory detection on spatial information processing (Harris et al. 2004) but also aids in explaining why we can promptly and precisely direct our response to a somatic stimulus from the external world (Brandes and Heed 2015).

Supplementary material

Supplementary material can be found at *Cerebral Cortex* online.

Funding

National Health Research Institutes of Taiwan (NHRI-EX106-10615NC); Ministry of Science and Technology of Taiwan (MOST

104-2314-B-002-044-MY3, 107-2314-B-002-073, and 108-2410-H-002-110-MY2).

Notes

We appreciate the support from the Imaging Center for Integrated Body, Mind and Culture Research in National Taiwan University. *Conflict of Interest*: The authors declare no competing financial interests.

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