Right parietal dominance in spatial egocentric discrimination

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**Abstract**

Egocentric tactile perception is crucial for skilled hand motor control. In order to better understand the brain functional underpinnings related to this basic sensorial perception, we performed a tactile perception functional magnetic resonance imaging (fMRI) experiment with two aims. The first aim consisted of characterizing the neural substrate of two types of egocentric tactile discrimination: the spatial localization (SLD) and simultaneity succession discrimination (SSD) in both hands to define hemispheric dominance for these tasks. The second goal consisted of characterizing the brain activation related to the spatial attentional load, the functional changes and their connectivity patterns induced by the psychometric performance (PP) during SLD. We used fMRI in 25 right-handed volunteers, applying pairs of sinusoidal vibratory stimuli on eight different positions in the palmar surface of both hands. Subjects were required either to identify the stimulus location with respect to an imaginary midline (SLD) to discriminate the simultaneity or succession of a stimuli pair (SSD) or to simply respond to stimulus detection. We found a fronto-parietal network for SLD and frontal network for SSD. During SLD we identified right hemispheric dominance with increased BOLD activation and functional interaction of the right supramarginal gyrus with contralateral intra-parietal sulcus for right and left hand independently. Brain activity correlated to spatial attentional load was found in bilateral structures of intra-parietal sulcus, precuneus extended to superior parietal lobule, pre-supplementary motor area, frontal eye fields and anterior insulae for both hands. We suggest that the right supramarginal gyrus and its interaction with intra-parietal lobule may play a pivotal role in the phenomenon of tactile neglect in right fronto-parietal lesions.

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**Introduction**

Among the somatosensory system functions, processing information about the location of tactile stimuli on the body surface is essential for motor control and action involving the body and limbs (Dijkerman and de Haan, 2007). Considerable knowledge has now been gained using tactile perception paradigms, demonstrating that when tactile tasks are performed accurately, activity increases in parietal (Binkofski et al., 1999; Bodegard et al., 2001; Seitz et al., 1991; Stilla et al., 2007) and prefrontal structures (Binder et al., 2004; Pleger et al., 2006; Stoeckel et al., 2003; Zhang et al., 2004). Some studies have focused on the attentional brain network during tactile perception, using the modulatory effects of the stimuli response as a measure of attention. Thus, previous works show that brain activity could be modulated by stimulus features in different perceptual modalities. Enhanced responses to attended tactile stimuli have often been observed in higher order parietal areas located along the intra-parietal sulcus and the medial wall of the pre-supplementary motor area (Albanese et al., 2009; Burton et al., 2008; Macaluso and Driver, 2001; Nachev et al., 2007; Stilla et al., 2007; Young et al., 2004).

While these studies have provided important insights on the understanding of the tactile attentional network, the modulation of this network activity and how the nodes of these circuits interact to process basic tactile discrimination of stimuli are still far from understood. In addition, most of the previous studies in tactile perception were carried out with unimanual paradigms. The use of a bimanual paradigm and the assessment of its differential effects on brain activity may reveal different organizational patterns for right/left limbs during the processing of tactile information. An improved understanding of the inter-hemispheric differences may help to elucidate the phenomenon of “spatial neglect,” characteristic of right fronto-parietal lesions (Leibovitch et al., 1998; Mort et al., 2003; Vallar and Perani, 1986) or hypoperfusion in the same brain structures (Hillis et al., 2005). Patients with unilateral brain lesions in the right hemisphere present abnormalities to report or respond to stimuli on the left side of the body or left-sided space, despite of the sensory input remaining intact (Buklina, 2002; Critchley et al., 1951). This phenomenon has also been associated to impairments of attentional processing (Heilman and Valenstein, 1979; Heilman and Watson, 1977), or impaired connectivity in the attentional network (He et al., 2007).

The current experiment investigates the activation of human cortical regions and their connectivity patterns that mediate two
types of tactile attention: the spatial localization and simultaneity succession discrimination of stimuli pairs on the palmar surface of the left and right hand, to assess the neural substrate and hemispheric dominance for these basic somatosensory perception tasks. Previous studies have linked the dysfunction in the spatial somatosensory attentional network of the right to the spatial neglect phenomenon (Heilman and Watson, 1977; Heilman and Valenstein, 1979). Hence we evaluated whether hemispheric differences in brain activity and connectivity patterns in healthy subjects may help to explain the tactile neglect phenomenon (Bisiach et al., 2004). This was carried out by varying parametrically the demands of spatial somatosensory attention.

We used a parametric design where the subject was required to spatially localize vibratory stimuli applied in different locations on the palm of the hand with respect to an imaginary midline, thus obtaining a gradation of localization uncertainty. The perceptual uncertainty may selectively modulate the spatial attention and sensory information processing load (Boultier, 1977), since it appears that spatial attention has the effect of increasing the spatial resolution of perception and of reducing the subject’s uncertainty in making judgements about a stimulus (Vecera and Rizzo, 2003) We used the subject’s performance during spatial location discrimination (SLD) as a regressor in a voxel-wise analysis. This approach allowed us to differentiate areas where neural activity co-varied with the subject’s performance, and therefore, brain activity modulations were related to egocentric spatial attention changes. To characterize functional interactions of the areas correlated with psychometric performance we used a psycho-physiological interaction (PPI) analysis (Friston et al., 1997). This analysis allowed us to make inferences about interregional interactions of the putative brain regions correlated to subject performance during perceptual egocentric tactile discrimination.

The design of our experiment was based on vibratory stimulation for studying the somatosensory system, as it was considered that this would be a more physiological tool than electrical stimulation. Devices producing high frequencies of vibratory stimulation have been used to generate robust BOLD responses (Francis et al., 2000; McGlone et al., 2002).

Materials and methods

Subjects

Twenty-five right-handed volunteers (Oldfield, 1971) of age ranging from 19 to 47 years (mean 28) were recruited among the students and working personnel of the University of Navarra. None of the subjects had a history of neurological or psychiatric illness. Prior to scanning, subjects gave written informed consent and the study had the approval of the local ethics committee.

Vibratory stimulation

We developed a computer-controlled MRI-compatible vibratory device made of 8 piezolectric bender elements (T220-H4-NM303 Standard Brass Shim Bending Element, Piezo Systems, Inc., Cambridge, MA). Each bender made mechanical contact with the skin through a 4 mm diameter shaft. The device electrically insulated the body from the driving voltage of the bender (± 180 V), reaching a free deflection of ± 300 μm with a blocked force of 0.23 N, which was sufficient to produce a supra-threshold perception (Mountcastle et al., 1972). The array of 8 plastic shafts were aligned and spaced 8 mm from each other and attached to the surface of the palm. This device was tested to tune configuration parameters such as stimulation frequency, inter-stimulus interval (ISI), stimulus duration, shaft diameter and location.

The vibratory stimuli were presented in pairs. Each stimuli pair was composed of two sinusoidal vibrations of 40 ms duration, separated by an inter-stimulus interval (ISI), which varied from 8 to 57 ms in 8 steps (8–12–17–23–30–38–47–57 ms). Each stimuli pair was delivered on the palm of the hand (see Fig. 1A), each time at one stimulation shaft, varying the 8 stimulus positions and the 8 ISIs in a pseudo-random design. The vibration frequency was 243 Hz, within the range for Pacinian and Meissner afferent excitation (Mountcastle et al., 1972; Vallbo and Hagbarth, 1968). This frequency was also chosen in order to avoid the harmonics of the electrical network (50 Hz). The vibratory device was attached to the palm of the stimulated hand with Velcro tape. Both the stimulator device and the response box were placed in a comfortable position for the subject using a Velcro band attached to the hip.

fMRI study

Study paradigm

The paradigm design consisted of three tasks: tactile stimuli detection (control), simultaneity–succession discrimination (SSD) and spatial location discrimination (SLD). The events corresponding to the experimental tasks and rest were presented in blocks of 6 (4 task and 2 idle events), with an inter-event interval of 4 s plus a random jitter 0–450 ms. Each pseudo-block contained events of one task only. Within each pseudo-block, the event type defined by position and ISI was varied pseudo-randomly. For detection, the subject was required to report stimulus detection, regardless of ISI and position. During SLD, the subject was asked to report whether the stimuli were located right or left with respect to an imaginary midline crossing the palm of the hand between ring and middle finger, ignoring the ISI. Finally, in the SSD task, subjects were asked to answer if they had perceived one or two vibratory pulses, regardless of position. For the three tasks, subjects had to report their answers by pressing a button with the index or middle finger of the opposite hand. The response box was placed in vertical position on the subject’s abdomen. For detection, subjects had to press the button alternatively (i.e. first vibratory pair = top button, second vibratory pair = down button, and so on during the four events of the pseudo-block). The experiment contained the same amount of vibratory stimulations and motor responses for each task.

The instructions indicating to the subjects which task they had to carry out were given by presenting visually the words ‘where?’ for SLD, ‘how many?’ for SSD or ‘alternate’ for detection. There were 64 events per task (SLD, SSD, detection and idle events) and per hand. The presentations of the three tasks varied pseudo-randomly within each run. The experiment was carried out by stimulating sequentially the right and left hands. The order of hand stimulation was counterbalanced among subjects.

Scanning protocol

Each subject underwent four fMRI scanning runs (two per hand). The presentation of the stimuli was designed using Matlab and Cogent 2000 (Wellcome Trust Center for Neuroimaging, 12 Queen Square, London). Eye movements were monitored using an eye-tracking device (Long Range Optics System, ASL, Bedford, MA).

Imaging was performed using a 3 T scanner (Siemens Trio TIM, Siemens AG, Erlangen, Germany) equipped with a 12-channel head array coil. The functional images sensitive to blood oxygenation level-dependent contrast (BOLD) were acquired using a T2*-weighted echo-planar imaging sequence. Each volume comprised of 50 transverse slices without gaps covering the whole brain. Other imaging parameters were: resolution = 3 mm isotropic, echo time (TE) = 30 ms, repetition time (TR) = 3.0 s. A total of 184 volumes were acquired per run in a scan time of 9 min. To avoid systematic relationships between slice acquisition and stimulus presentation, the stimulus onset was randomly jittered with respect to the beginning of each volume acquisition. The first 3 volumes of each session were discarded and did not enter the analysis. Anatomical images were
acquired with a MPRAGE sequence, with the following imaging parameters: resolution = 1 mm isotropic, FOV = 192 × 256 mm², matrix = 192 × 256, 160 axial slices, TR/TE/TI = 1620/3.87/950 ms, flip angle = 15°.

**Data analysis**

**Performance data analysis**

The performance variables response time (RT) and response consistency were evaluated. RT was defined as the time interval between the end of the stimuli pair application and the onset of the key press on the response box. Differences in RT due to task were evaluated using ANOVA (RM-ANOVA), and post-hoc comparison tests were done using a Bonferroni correction. Differences in RT during the SLD task due to hand or position were evaluated using a two-factor RM-ANOVA.

The response consistency of each subject for each stimulation position in the SLD task was evaluated using a consistency index (CI). This was calculated following the equation $CI = \frac{abs(r_1 - r_2)}{r_1 + r_2}$ (Pastor et al., 2004), where $r_1$ and $r_2$ corresponded to the number of left and right answers, respectively. The CI quantifies the difference between the relative frequencies of the responses for each subject and stimulation position. Thus is within the range values between 0 and 1.

Differences in consistency due to hand or position were evaluated using a two-factor RM-ANOVA. The CI was used to identify two categories in the SLD task (see Results section): one category for which subjects responses were highly consistent (when the stimuli were applied in positions 1, 2, 7 and 8, see Fig. 1B) and a second category for which responses were not consistent (when stimuli were applied in positions 3, 4, 5 and 6).

Eye-tracker data were continuously recorded, for control of attention and sleepiness.

**Imaging data analysis**

We used Statistical Parametric Mapping (SPM5) software for image processing and analysis (http://www.fil.ion.ucl.ac.uk/spm). For each subject, the 368 volumes of the two sessions per hand were realigned to the first image, sync-interpolated over time to correct for phase advance during volume acquisition, coregistered with the anatomical image and normalized to the Montreal Neurological Institute reference brain. Data were spatially smoothed with an 8 mm isotropic Gaussian filter and filtered in time using a high-pass filter of 128 s.

We used a two-level analysis procedure for statistical inference at a random effect level (Penny et al., 2003). In the first-level analysis, the time series of each subject were analyzed separately for each hand. The 24 event types (i.e., 8 for detection, 8 for SLD and 8 for SSD) were modeled with a canonical double gamma for hemodynamic response function (HRF).

**Brain activation patterns during SLD and SSD**

First, we estimated the following two contrasts of interest: SLD vs. detection and SSD vs. detection. For these contrasts, group t-maps were generated by applying the one-sample t-test for the contrast parameter values of all the subjects at each voxel (degrees of freedom = 24). Differences in brain activation between right and left hand stimulation during SLD and SSD were assessed at the group level using a two-way within-subject ANOVA with the factors hand and task to compare the individual contrast maps (SLD vs. detection and SSD vs. detection) obtained for each stimulated hand.

**Brain activation patterns during low and high consistency trials in the SLD task**

At the first level analysis, individual contrast images were generated by subtracting SLD vs. detection for events presented in each stimulation position separately. In this case 16 contrast images were generated per subject (8 images per stimulated hand). At the second level, these individual contrast images were entered into a two-way ANOVA, with the factors hand and stimulus position. Group brain activation maps obtained for each stimulated hand were classified in low and high consistency trials, respectively, using T contrasts. For this contrast we considered high consistency trials the stimuli presented in 1, 2, 7 and 8 positions, and low consistency trials in stimulus positions 3, 4, 5 and 6. Subsequently, conjunction analyses with conjunction null hypothesis were carried out to evaluate areas common to both hands.

To assess differences in brain activity levels between low and high consistency trials in the SLD task, an additional model was specified using the individual CI for spatial discrimination as regressor in the
design matrix, for stimulation on the left and right hand separately. Thus, for each subject t-contrast images were computed for the positive (+1) and negative (−1) effect of the regressor. The positive effect of the regressor yielded brain areas where neural activity positively correlated with the subject’s performance (CI) (i.e. areas where neural activity was higher during high consistency trials and lower during low consistency trials). The negative slope of the regressor showed brain areas where neural activity correlated negatively with CI (i.e. areas where neural activity was higher during low consistency trials and lower during high consistency trials). Activity increases during low consistency trials are induced by the increased difficulty of the SLD task, as the stimulation position is approaching the reference midline, thus increasing the cognitive demand and spatial attention load of the task.

The individual maps obtained from these contrasts were entered in a one-way ANOVA, with the factor hand. Differences in BOLD signal correlation with consistency index between stimulated hands were assessed. Subsequently, we used conjunction analyses (Price and Friston, 1997) to define areas correlated with performance (CI) during SLD common to both stimulated hands.

The significance threshold for all random effect analyses was set at $p < 0.05$, FDR corrected for multiple comparisons (Genovese et al., 2002), with a minimum cluster size of 10 voxels. In the comparisons where no voxel exceeded a corrected map-wise level of significance, we set an uncorrected significance level at $p < 0.001$ (which is equivalent to $t > 3.11$) and a cluster size $> 10$.

Effectiveness connectivity analysis

The analysis of effective connectivity assesses the hypothesis that activity in one brain region can be explained by an interaction between the presence of a cognitive process and activity in another part of the brain. We used the psycho-physiological interactions (PPI) method (Friston et al., 1997) to estimate effective connectivity changes for brain structures where neural activity increased during the low consistency trials in the SLD task.

We selected from the group map obtained in the negative correlation analysis with CI the three main clusters as initial seeds, based on: the cluster size, the level of significance and the cluster relevance during perceptual decision making, according to the literature (Albanese et al., 2009; Burton et al., 2008; Macaluso and Driver, 2001; Nachev et al., 2007; Stilla et al., 2007; Young et al., 2004). These regions increased their activity as the spatial attention load of the task increased. The regions were: pre-supplementary motor area (BA6a); the anterior ventral bank of the intra-parietal sulcus (hIP1) (Caspers et al., 2008; Choi et al., 2006) contralateral to the stimulated hand and precuneus (BA7) above the intra-parietal sulcus.

The PPI method is an exploratory multi-regression analysis that consists of a linear combination of 4 terms that can be denoted as $y_1 = \beta_0 + b(y_0 \times u) + cu + X\beta$, as described by (Stephan, 2004). The task regressor $u$ is the psychological variable (here the degree of localization uncertainty during SLD as measured by response consistency [CI]), the time series $y_0$ is the physiological variable acting as the seed of the analysis, the PPI regressor $y_0 \times u$ is a bilinear term formed by the product element-by-element of the task regressor and the seed time series and a constant term formed by the product element-by-element of the task regressor $u$ and the seed time series and a constant term.

At individual level, two t-contrasts were created that were 1 and −1 for the PPI regressor, respectively, and 0 elsewhere. Testing for the positive slope of the regressor (contrast weight 1) yielded areas that increased connectivity with the seed area during high consistency trials with respect to low consistency trials. Conversely, testing for the negative slope of the regressor (contrast weight −1) yielded areas that increased connectivity with the seed area during low consistency trials with respect to high consistency trials.

Subsequently, conjunction analyses were carried out to assess changes in connectivity common to both stimulated hands.

Results

Performance data

Subjects performed a tactile discrimination task with vibratory stimuli in separate sessions for each hand. They were asked to respond to three different tasks: detection, SLD and SSD. There was a significant effect of task in RT measurements ($F(2,147) = 34.449; p < 0.0001$). Post-hoc tests revealed that RT was significantly shorter during detection than during the SLD or SSD tasks ($p < 0.0001$; RT$_{detection} = 794.4 \pm 186.8$ ms (mean ± SD); RT$_{SLD} = 1061.6 \pm 164.7$ ms; RT$_{SSD} = 1078.6 \pm 220.4$). During the SLD task, there was a significant effect of position ($F(7,384) = 19.065; p < 0.0001$), but there was no significant effect of hand ($F(1,384) = 2.558; p = 0.111$) and no interaction between hand and position ($F(7,384) = 0.649; p = 0.715$).

Behavioral analysis of SLD responses showed that for those stimuli pairs presented closer to the virtual midline of the palm (positions 3, 4, 5 and 6), subjects’ responses were variable, while for lateral presentations, distant from the midline (positions 1, 2, 7 and 8), they were consistent (see Fig. 1B) for both right and left hand stimulation. The consistency index thus measured the degree of uncertainty in the spatial localization of the stimuli. Spatial discrimination close to threshold is more demanding of spatial attention even though the subjects receive the same type and number of stimuli. The CI also reflects the increase in cognitive demand to perform the same task when the stimulation position is close to the virtual reference. The consistency index did not change with the stimulated hand ($F(1,384) = 2.513; p = 0.114$), but there were significant differences due to stimuli location ($F(7,384) = 25.602; p < 0.0001$). There was no significant interaction between stimulated hand and stimuli location ($F(7,384) = 0.917; p = 0.493$).

fMRI data

SLD vs. detection

For SLD relative to detection, the pattern of brain activity for stimulation on the right hand was mainly bilateral in parietal and prefrontal regions. During stimulation on the left hand, significant brain activity was found mainly in contralateral superior and inferior parietal lobule and ipsilateral prefrontal regions (Fig. 2A and B, Table 1A). Significant differences between hands were found mainly in right prefrontal and left parietal regions, with the global maxima located in the right supramarginal gyrus. Detailed brain differences are expounded in Table 1B and Fig. 2C. These regions were more active during right compared with left hand stimulation. We did not find significant differences for left compared to right hand stimulation ($P_{unc} < 0.001$).

SSD vs. detection

Brain activity patterns during SSD were similar for left and right hand stimulation. During stimulation on the right/left hand the SSD vs. detection contrast yielded brain activity mainly in bilateral insulae and midline structures: middle cingulate cortex extended to medial superior frontal gyrus and supplementary motor area (expanded information is in Table 3 of supplementary material for the left and right hand stimulated). Results for SSD vs. detection were in agreement with previous findings of Pastor and collaborators (2004). In contrast to SLD, we did not find significant differences in the activation maps comparing both hands ($P_{unc} < 0.001$).

It is important to note that although differences in response times of discrimination tasks and detection may have influenced the subtraction of the task and control. However the magnitude of these
differences of about 300 ms has minimal repercussion in an event-related fMRI experiment due to the low temporal resolution of this technique.

Brain activity during the high consistency trials of the SLD task

Conjunction analysis of both hands during the high consistency SLD events (i.e. the more evident presentations) revealed brain activity in bilateral parietal structures including bilateral precuneus, superior and inferior parietal lobule, supramarginal gyrus, right precuneus (maximum cluster), and subcortical structures. Detailed information is detailed in Fig. 1A and Table 1 of supplementary material.

Brain activity during the low consistency trials of the SLD task

Conjunction analysis of both hands during low consistency trials (i.e. the more ambiguous presentations) revealed neural activity in the same brain structures active during the more evident presentations, plus additional parietal and prefrontal structures as depicted in Fig. 1B of supplementary material. Detailed information about these findings is detailed in Table 1 of supplementary material.

Regression analysis with consistency index (CI)

The consistency index measured the degree of uncertainty in the spatial localization of the stimuli. The CI decreased when the stimulation position was closer to the virtual reference. A negative correlation between BOLD signal and CI in a specific brain region can be interpreted as an increase in neural activity induced by the increase in spatial attention demand of the task as the stimulus localization becomes ambiguous.

Conjunction analysis of right and left hand stimulation showed brain activity negatively correlated with consistency index in pre-supplementary motor area. The cluster was located in the mesial superior frontal gyri and rostrally to the vertical anterior commissure, anatomically coincident with Brodmann Area 6a/b (Nachev et al., 2008; Picard and Strick, 1996) in both hemispheres, extended to middle cingulate cortex. Other bilateral structures were the intraparietal sulcus: hIP1 extended to hIP2 and inferior parietal lobule (BA40), superior parietal lobule (BA7), precuneus (BA7), frontal eye fields, insulae and postcentral gyrus; left cerebellum (VI) and crus 1; (see Table 2A for detailed information). The conjunction analysis of SLD in both hands is presented in Fig. 3.

The main areas with positive correlation with consistency index were found in rostral anterior cingulate cortex, right posterior cingulate cortex, left middle temporal gyrus, right hippocampus and bilateral middle temporal gyrus. We found no significant differences among stimulated hands. Brain activity maps of positive correlation with CI result of right and left hand stimulation conjunction analysis are presented in supplementary material (Table 4).

Effective connectivity analysis (PPI)

We performed PPI analyses to study the interaction of the main clusters related to low CI during SLD. We chose as initial seed the three regions with the highest negative correlation (i.e. higher activity during low consistency trials): pre-supplementary motor area, the intraparietal sulcus (hIP1) and precuneus contralateral to the stimulated hand. The results shown were obtained from conjunction analyses of both hands.

The PPI results revealed that some brain regions exhibited stronger connectivity with the seed during low consistency trials than high consistency trials and vice versa (i.e. other regions exhibited stronger connectivity with the seed during high than low consistency trials). In the first case, the increased connectivity could be induced by the increase in spatial attention demand by the task, when the stimulus localization is uncertain.

Seed on pre-supplementary motor area

Brain regions that exhibited significantly stronger connectivity with pre-supplementary motor area during low consistency than with high consistency trials were: bilaterally inferior parietal lobules, superior parietal lobule, superior frontal gyrus (frontal eye fields), left supramarginal gyrus, right precuneus and right Cerebellum (VIII) (Figs. 4A and 5B). All these areas including the seed (pre-supplementary motor area) showed an enhanced activity when the spatial attention load was increased.

Brain regions that had significantly stronger connectivity with pre-supplementary motor area during high consistency trials were found
Areas where BOLD signal correlates with CI (F<sub>vox</sub> < 0.05, k > 10)

Table 1

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B

Differences between right-left hand for SLD→detection (P<sub>contra</sub> < 0.001, k > 10)

Table 2

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<tr>
<td>Left supramarginal gyrus (BA2)</td>
<td>−60</td>
<td>−22</td>
</tr>
<tr>
<td>Left postcentral gyrus</td>
<td>−36</td>
<td>−30</td>
</tr>
<tr>
<td>Left precentral gyrus (BA6)</td>
<td>−34</td>
<td>−18</td>
</tr>
<tr>
<td>Right supramarginal gyrus (h)</td>
<td>54</td>
<td>−42</td>
</tr>
<tr>
<td>Right IPL</td>
<td>58</td>
<td>−42</td>
</tr>
<tr>
<td>Right IFG (paris triangularis)</td>
<td>36</td>
<td>28</td>
</tr>
<tr>
<td>Right middle frontal Gyrus</td>
<td>28</td>
<td>52</td>
</tr>
</tbody>
</table>

Discussion

The accurate spatial encoding of one's own body surface provides essential information for motor action. Thus, identifying the neural substrate of spatial localization of hand tactile stimuli is very important for the understanding of skilled movement awareness and hand motor control.

The design of this egocentric perception experiment for both hands allowed us to evaluate differential brain activity patterns during left and right hand stimulation and their relationship with the tactile neglect phenomenon. Additionally, the covariation of brain activity with subject's behavior and the connectivity changes assessed in the main structures associated to the ambiguity of the task, allowed a better understanding of the hemispheric predominance of the network related to tactile perception of the own body.

Areas activated for egocentric spatial discrimination and their relationship with spatial neglect

Our results show that during spatial localization on the right hand compared to the left hand, clusters of enhanced neural activity were found in both hemispheres, with the global maxima in the right supramarginal gyrus extended to inferior parietal lobule. (Figs. 4D and 5A).

Brain regions that had significantly stronger connectivity with contralateral hIP1 during high consistency trials were linguistic gyrus supplementary eye fields (Grosbras et al., 1999), left medial superior frontal gyrus, left superior temporal gyrus extended to left Rolandic operculum (OP1) and right medial precuneus. (Figs. 4C and 5A).

Seed on contralateral precuneus

Seeding on contralateral precuneus, we found significantly stronger connectivity with left middle superior frontal gyrus and bilateral lingual gyrus during high consistency trials (Figs. 4E and 5A).

We did not find significant interactions with any brain area during low consistency trials.

Detailed information about the brain structures that exhibited significant connectivity changes with the seed in each case is included in Table 2 of supplementary material.

mainly in midline structures: right rostral anterior cingulate extended to middle orbital gyrus, which exhibited a decreased activity when spatial attention load was increased (Figs. 4B and 5B).

Seed on contralateral intra-parietal sulcus (hIP1)

Brain regions that had significantly stronger connectivity with contralateral hIP1 during low consistency trials were found only in the right supramarginal gyrus.
inferior parietal lobule (supramarginal gyrus). Other clusters were located in left parietal and right prefrontal areas. These brain activity differences were present even though no significant differences in behavior were found between right/left hand stimulation. Brain activity in these parietal regions also showed negative correlation with CI, implying that activity levels were associated to spatial attentional load. This differential pattern shows therefore that spatial localization on the right hand recruited neural activity in both parietal lobules; meanwhile, spatial localization on the left hand recruited activity predominantly in the right parietal lobe. This indicates that information processing related to personal space and spatial attention on the right hand, in right-handed subjects, is supported by both hemispheres. Nevertheless their left hand is mainly controlled by the contralateral hemisphere. This differential activation could contribute to clarify the origin of somatosensory neglect predominant in the left hemibody as a result of right fronto-parietal lesions (Berti et al., 2005; Bisiach et al., 1990; Bukлина, 2002; Robertson and North, 1992). When the lesion affects the left hemisphere, the ipsilateral right parietal could exert a functional supply for lesions located in left parietal areas. In addition, anatomo-clinical data suggest that lesions in the posterior parietal lobe correlate with visuo-spatial unilateral neglect, being the crucial area the right supramarginal gyrus (BA40) (Leibovitch et al., 1998; Vallar and Perani, 1986). Moreover, egocentric neglect was strongly associated with hypoperfusion in the supramarginal gyrus in visual modalities (Hillis et al., 2005). Despite that the role of the supramarginal gyrus in tactile processing information has not been emphasized in the literature, there is some evidence of increased activity of the supramarginal gyrus during tactile processing in blind subjects (Burton et al., 2004). It is worth to notice that in our work the cluster of maximum activity enhancement on the right vs. left hand stimulation was located in the right supramarginal gyrus. In addition, the connectivity results show that both intra-parietal sulcus contralateral to the stimulated hand gain connectivity with the right supramarginal gyrus during low consistency trials. This suggests that the right supramarginal gyrus has a role in personal space information processing related to both limbs and that this role is crucial when the
spatial attentional load is increased. Thus, results reported in this experiment support the hypothesis that egocentric tactile neglect may be associated with a dysfunction of the right supramarginal gyrus (BA40) or the disruption of connectivity between this area and the intra-parietal sulcus.

Effects of spatial attention load on tactile spatial processing

The brain regions activated during the more consistent tactile spatial localizations were principally two bilateral clusters in the parietal cortex: one in the posterior part of the superior parietal lobule, and another in the intra-parietal sulcus (hIP1) extended to hIP2 and inferior parietal lobule and a third one in the right precuneus, independently of the right/left hand stimulated. These results are in agreement with previous findings (Stilla et al., 2007) which suggest that activity in the right posterior intra-parietal sulcus and right precuneus increases with accuracy in tactile discrimination. When the ambiguity in the perception of the stimulus location increased, as shown by a reduced consistency index, activity in most of these areas experienced a significant enhancement, and there was an additional recruitment of bilateral prefrontal structures (pre-supplementary motor area, frontal eye fields, anterior insulae and dorso-lateral prefrontal cortex). Some studies have linked posterior and anterior parietal cortex, pre-supplementary motor area and anterior insulae to tactile attention (Burton et al., 1999, 2008), similar brain regions were found responsible for visuo-spatial attention (Kastner et al., 1999; Moore and Armstrong, 2003).

The connectivity analysis showed different connectivity patterns during the low and high consistency trials in SLD. As reported in other experiments during both motor (Pe:\tt\text{\textit{fier et al., 2005; Wu et al., 2008}}) and visual tasks (Bavelier et al., 2000; Buchel and Friston, 1997), the connectivity pattern varies dynamically as a function of the ongoing cognitive demands. Thus, we can infer that increases in the spatial attention load during tactile localization induced changes in functional connectivity, that were found mainly in the brain structures which actively took part in the SLD task: pre-supplementary motor area, contralateral intra-parietal sulcus and precuneus. Interestingly, these three areas showed a loss of connectivity with prefrontal and midline structures which belong to the “default mode” and were not involved in the tactile spatial localization task (targets of the green lines in Fig. 5). This loss of interaction may be due to the increased involvement of this fronto-parietal network in the SLD task as the spatial attention load increases.

Among the multiplicity of functions attributed to pre-supplementary motor area, a role proposed by Seitz et al. (2009) is that it may exert a top-down modulation of lower-order cortical sensory areas during the process of perception. In our experiment, during the more evident discrimination events (high consistency trials) only the precuneus, the posterior part of the superior parietal lobule and the hIP1 extended to hIP2 were active. When the ambiguity of the task increased (low consistency trials), the pre-supplementary motor area became active during the task. Additionally, it showed a decrease of interaction with midline structures, but a gain in connectivity with parietal regions and frontal eye fields (targets of the magenta lines in Fig. 5). These results support a fundamental role of pre-supplementary motor area, which operates giving relevance to parietal and prefrontal structures, to improve the efficiency of the localization when the spatial attentional load is increased.

Temporal tactile processing

For SSD compared to detection, our results revealed similar activity patterns during stimulation of both hands. This pattern consisted of a frontal network made up by pre-supplementary motor area, anterior cingulate cortex and bilateral anterior insulae. These results confirmed previous findings obtained with paired electrical stimulation (Pastor et al., 2004), where pre-supplementary motor area and anterior cingulate cortex were found to play a pivot role during temporal tactile processing. The results support also the hypothesis that SSD relies on a central processor multimodal (Pastor et al., 2004, 2006), independent of the stimulated hand and associated with sensorimotor control, whereas self-body spatial perception has a hand-dependent domain.

In conclusion, this approach allowed us to differentiate two brain activity patterns: a fronto-parietal with greater extent of activation in the right than in the left hemisphere which is active during SLD, and another prefrontal without hemispheric differences which process the SSD. This experiment, which was focused to test the same
perceptual spatial discrimination task for the right and left hand, revealed two highly significant aspects. First, the hemispheric specialization, with the crucial role of the right supramarginal gyrus. This finding gives a clue to the origin of tactile neglect in right fronto-parietal lesions. Second, the important function of pre-supplementary motor area, which through its connectivity pattern may be exerting control over the activity modulations related to spatial attentional load.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.neuroimage.2010.12.011.

References