The contribution of primary and secondary somatosensory cortices to the representation of body parts and body sides: an fMRI adaptation study

Luigi Tamè[1,2], Christoph Braun[1,3,4], Angelika Lingnau[1], Jens Schwarzbach[1,3], Gianpaolo Demarchi[1], Yiwen Li Hegner[4], Alessandro Farnè[5,6] and Francesco Pavani[1,3]

1. Center for Mind/Brain Sciences, University of Trento, Rovereto, Italy

2. School of Psychology and Clinical Language Sciences, University of Reading, Reading, UK

3. Dep. of Cognitive Sciences and Education, University of Trento, Rovereto, Italy

4. MEG-Center, University of Tübingen, Germany

5. INSERM U1028, CNRS UMR5292, Bron, F-69500, France

6. Université Claude Bernard Lyon I, Lyon, F-69000, France

Address for correspondence:

Luigi Tamè

Center for Mind/Brain Sciences, University of Trento

Corso Bettini 31, 38068 Rovereto, Italy

Phone: +39 0464 808674. Fax: +39 0464 808602

E-Mail: luigi.tame@unitn.it l.tame@reading.ac.uk

Running head: fMRI-A OF FINGER REPRESENTATIONS

Abstract

While the somatosensory homunculus is a classically used description of the way somatosensory inputs are processed in the brain, the actual contribution of primary (SI) and secondary (SII) somatosensory cortices to the spatial coding of touch remains poorly understood. We studied adaptation of the fMRI BOLD response in the somatosensory cortex by delivering pairs of vibrotactile stimuli to the finger tips of the index and middle fingers. The second stimulus (test) was always administered to the left index finger, while the first stimulus (adaptor) was delivered either to the same or to a different (middle) finger of the right or left hand. The overall BOLD response evoked by the stimulation was primarily contralateral in SI and was more bilateral in SII. However, our fMRI adaptation approach also revealed that both somatosensory cortices were sensitive to ipsilateral as well as to contralateral inputs. SI and SII adapted more when the stimulation repeated over homologous than non-homologous fingers, showing a distinction between different fingers. Most importantly, for both somatosensory cortices this finger-specific adaptation occurred irrespective of whether the tactile stimulus was delivered to the same or to different hands. This result implies integration of contralateral and ipsilateral somatosensory inputs in SI, as well as in SII. These findings suggest that SI is more than simply a relay for sensory information, and that both SI and SII contribute to the spatial coding of touch by discriminating between body parts (fingers) and by integrating the somatosensory input from the two sides of the body (hands).

Introduction

When coding the location of a tactile stimulus on the body, our brain needs to determine which body part and which body side was stimulated. This spatial disambiguation likely begins with neural processing in primary (SI) and secondary (SII) somatosensory cortices. The contribution of SI to the representation of *body parts* has been well-established since the classical studies of Fritsch and Hitzig (1870) in dogs, and the pioneering studies of Penfield and colleagues in humans (e.g., Penfield & Rasmussen, 1950). Many subsequent studies have confirmed the somatotopic organisation in SI in humans using neuroimaging techniques (e.g., Nelson, & Chen, 2008; Overduin, & Servos, 2004; Sanchez-Panchuelo, Francis, Bowtell, & Schluppeck, 2010). Moreover, there is now evidence that a somatotopic organisation also exists in SII, albeit to a lesser degree (e.g., Del Gratta, Della Penna, Ferretti, Franciotti, Pizzella, Tartaro, Torquati, Bonomo, Romani, & Rossini, 2002; Ruben, Schwiemmann, Deuchert, Meyer, Krause, Curio, Villringer, Kurth, & Villringer, 2001). The textbook description of the somatosensory cortices identifies SI as a cortical area with primarily contralateral afferents, whereas SII is an area in which bilateral afferents are denser. This suggests that integration of the somatosensory inputs from the two body sides should occur in SII, but not in SI. Thus, the contribution of the somatosensory cortices to the representation of the two *body sides* appears straightforward.

However, neurophysiological studies in monkeys and neuroimaging works in humans have recently challenged the notion that neural representations of the body in SI are purely contralateral (e.g., Sutherland, 2006). In monkeys, bilateral receptive fields have been found within SI, in Brodmann's area 2 (Iwamura, Taoka, & Iriki, 2001; Iwamura, Tanaka, Iriki, Taoka, & Toda, 2002). In humans, neuroimaging studies have documented neural activity in SI in response to tactile stimulation on the ipsilateral side of the body (e.g., Hlushchuk, & Hari, 2006; Kanno, Nakasato, Nagamine, & Tominaga, 2004; Tommerdahl, Simons, Chiu, Favorov, & Whitsel, 2006). Behavioural studies in humans also corroborate the notion that SI may hold sensory

representations that are not fully separated between body sides. For instance, tactile localization errors at the hands, which reflect the somatotopic organization in SI (Schweizer, Braun, Fromm, Wilms, & Birbaumer, 2001), can be modulated by applying tactile stimuli to the fingers of the opposite hand (Braun, Hess, Burkhardt, Wühle, & Preissl, 2005). Similarly, participants trained to discriminate punctuate pressure or roughness stimuli on one finger of the right hand (e.g., the index) can transfer this training to the first neighbouring finger of the same hand (i.e., the right middle finger) as well as to the homologous finger of the opposite hand (i.e., the left index finger; Harris, Harris, & Diamond, 2001). Finally, clear interactions between tactile stimuli delivered to opposite body sides were recently documented in a paradigm of tactile double simultaneous stimulation (DSS) at the hands (Tamè, Farnè, & Pavani, 2011), in which participants detected tactile stimuli at a pre-defined target finger that could be stimulated alone or concurrently with another finger, either on the same or the opposite hand. For instance, when the target finger was the right index, the concurrent stimulation could be presented to the middle finger of the same hand, to the left index finger or to the left middle finger. The results showed interference effects of tactile DSS both within and between hands, which were more dependent upon the identity of the stimulated body-part (i.e., which finger was touched) than body-side (i.e., which hemibody was touched). These findings imply that at least some aspects of the processing of concurrent or subsequent tactile stimuli are integrated across body sides.

In the present study, we examined the contribution of SI and SII to the spatial coding of touch at the fingers of the same or different hands, taking advantage of the fMRI adaptation paradigm. The adaptation paradigm relies on the hypothesised decrement of a neuronal response that results from the repeated presentation of a stimulus feature to which the neurons are selective. For instance, a population of neurons in the visual pathway selective to upward motion of visual stimuli would decrease its overall neuronal activity when the sequence of repeated stimuli contains the same feature (i.e., upward motion). This physiological response was initially

described in single cell recordings (e.g., Gross, Rocha-Miranda, & Bender, 1972; Tanaka, Saito, Fukada, & Moriya, 1991), and has now been largely documented also using fMRI (e.g., Brozzoli, Gentile, Petkova, & Ehrsson, 2011; Grill-Spector, & Malach, 2001; Krekelberg, Boynton, & van Wezel, 2006; Vuilleumier, Henson, Driver, & Dolan, 2002; Lingnau, Ashida, Wall, & Smith, 2009). In the present study, we examined adaptation when successive vibrotactile stimuli were delivered to the same or to different body parts (index or middle fingers), either on the same or on different body sides (left or right hands). Specifically, four different stimulation conditions were used (see Figure 1): (1) repeated unilateral stimulation of the same finger (i.e., left index finger, condition Li-Li; Figure 1a); (2) repeated unilateral stimulation of non-homologous fingers (i.e., left middle and left index fingers, condition Lm-Li; Figure 1b); (3) repeated bilateral stimulation of homologous fingers (i.e., right index and left index fingers, condition Ri-Li; Figure 1c); (4) repeated bilateral stimulation of non-homologous fingers (i.e., right middle and left index fingers, condition Rm-Li; Figure 1d). Note that the second stimulus (test) was always on the left index finger.

< Please insert Figure 1 about here >

We hypothesised that any brain areas that contain distinct neuronal populations for the index and middle fingers should adapt more when the index finger is stimulated twice as compared to when the middle and index fingers are stimulated in sequence. We expected this finger-specific adaptation in SI, which holds a strong somatotopic representation, and possibly to a lesser extent also in SII. Crucially, any brain area that integrates somatosensory inputs from the two hands should reveal finger-specific adaptation regardless of whether the stimulation occurs unilaterally or bilaterally. This finding should emerge in SII, which classically holds bilateral representations of somatosensory stimuli. However, it should emerge also in SI if a neural population that integrates inputs from the two sides of the body exists in this brain area.

Materials and Methods

Participants

Eighteen participants (mean age = 29, SD = 5 years; 7 females and 11 males) participated in the study. All reported normal or corrected to normal vision and normal somatosensation. Participants reported no history of psychiatric or neurological disorders, and no current use of any psychoactive medication. All subjects were right-handed according to their self-report. Participants gave their written informed consent prior to their participation in the study, which was carried out according to the principles of the Declaration of Helsinki, and was approved by the ethical committee of the University of Trento. One participant was discarded from the analysis because of several large, rapid head movements (> 6 mm).

Apparatus & procedure

During the experimental session the subject's unseen hands rested palm down in a comfortable posture, one on each side of their abdomen. Subjects were instructed not to touch their hands together in order not to form a loop with their arms that might lead to the induction of electrical currents. Tactile stimuli were delivered to the index and middle fingertips of either hands using four MR compatibles vibrators (Quaerosys, Schotten, Germany). To avoid possible distortions caused by the stimulation equipment in the MR environment, a ferrite low-pass filter was applied to the signals entering the MR room. The stimulator consisted of a single rod (1 mm in diameter), protruding from a flat surface of 4 x 8 mm. The rod protruded and retracted at 20 Hz for 1000 ms, producing clearly perceivable skin indentations. Wave signal intensity was always set to the maximum level available except for 8% of the trials, which were delivered at half-maximal intensity and served as fillers for the behavioural task. Vibrotactile stimulators were attached to the finger pads of the middle and index fingers of both hands using Velcro tape, to

ensure constant contact force between the fingers and the stimulation devices throughout the experiment.

Visual stimuli were delivered using a liquid-crystal projector (refresh rate: 60 Hz; resolution: 1280 x 1024 pixels) and were visible to the participants through a mirror positioned above the head coil. A fixation cross was presented at the centre of the screen: the cross was green during the vibrotactile stimulation period, and grey during the rest period. Occasionally, a written question appeared on the screen for 3000 ms probing the participants to answer whether they had just perceived a weak stimulation at the target finger.

Visual and vibrotactile stimulations were programmed using the in-house software "ASF" (Schwarzbach, in press), based on the MATLAB Psychotoolbox-3 (Brainard, 1997) for Windows. A response box (Lumina LP-400 system by Cedrus) was placed within reaching distance of the participant's right hand. Subjects were instructed to press the button with the right thumb in response to the question presented on the screen. Closed-ear headphones (Serena Sound digital-system: Resonance Technology Inc. California, U.S.A) were used for reducing noise caused by the operation of the scanner. The noise made by the operation of vibrotactile stimulators was not audible.

fMRI adaptation paradigm

The experiment consisted of 4 event-related fMRI adaptation scans, consisting of 52 trials each. In each scan, the 4 experimental conditions were repeated 12 times resulting in 48 trials, and responses to fillers were probed in 4 additional trials. Responses in the filler condition were excluded from further analyses.

At the beginning of each trial a green fixation cross appeared at the centre of the screen, and remained visible for the entire duration of the trial. 1000 ms after the appearance of the fixation cross, two consecutive vibrotactile stimuli were delivered to the participant's fingers, each lasting 1000 ms (S1, adaptation stimulus; S2, test stimulus). S1 and S2 were separated by an inter-

stimulus interval (ISI) of 1200 ms. After the presentation of S2 there was an inter-trial interval (ITI) ranging randomly from 6000 to 8000 ms. 3000 ms after the end of S2 the green fixation cross turned grey to inform the participant of the end of the trial. A schematic description of the trial structure is shown in Figure 2.

< Please insert Figure 2 about here >

Participants were instructed to pay attention to the left index finger throughout the experiment. To ensure that subjects were following the instructions, a written question appeared on the screen ("Did you feel the weak stimulation on your left index finger?") in four trials per scan, for a total of 16 trials in the whole experiment, excluded from the analysis.

The four experimental conditions were presented in a pseudo-random series. Specifically, it was assured that each condition was preceded equally often by any of the other conditions, including itself (Kourtzi, & Kanwisher, 2000). Conditions that included the written question were randomly integrated in the sequence. At the start and at the end of each scan a black-screen was presented for 16 and 20 seconds, respectively.

Data acquisition

MR scans were acquired using a 4T BrukerMedSpecBiospin MR scanner and an 8-channel birdcage head coil. Functional images were acquired using T2*-weighted gradient-recalled echo-planar imaging (EPI). An additional scan was performed to measure the point-spread function (PSF) of the acquired sequence, which served for the correction of the distortions expected with high-field imaging (Zeng, & Constable, 2002). We used 31 slices, acquired in ascending interleaved order providing almost full-brain coverage, with a TR (repetition time) of 2200 ms (voxel resolution: 3 x 3 x 3 mm; TE (echo time): 33 ms; flip angle (FA): 75°; field of view (FOV): 192 x 192; gap size: 0.45 mm). In addition, a fat saturation (FS)

pulse was used to avoid EPI artefacts. Each participant performed 4 EPI scans, with the number of volumes varying between 360 and 391. These variations were due to the partially randomised duration of the ITI in the trial generation, creating a small variation in the number of volumes acquired across scans and participants.

In order to perform the coregistration between low-resolution functional and high-resolution anatomical images, we acquired a T1 weighted anatomical scan (MP-RAGE; 1 x 1 x 1 mm; FOV: 256 x 224; 176 slices; GRAPPA acquisition with an acceleration factor of 2; TR: 2700 ms; TE: 4.18 ms; inversion time (IT): 1020 ms; 7° flip angle) for each participant.

Data analysis

Data analysis was performed using BrainVoyager QX 2.0 (Brain Innovation, The Netherlands). Prior to analysis, the first two volumes of the functional data of each scan were discarded. Distortion correction was applied on the basis of the PSF, acquired before each EPI scan, to correct distortion derived from the EPI images. Functional data preprocessing was performed applying a three-dimensional (3D) motion correction referred to the first volume in the scan and a temporal high-pass filter with a cut-off of 3 cycles/scan. A Gaussian kernel of 4.5 mm was applied tosmooth the images spatially. Next, functional data were co-registered with a high-resolution de-skulled anatomical scan for each participant in their native space. For group analysis, echo-planar and anatomical images were transformed into Talairach & Tournoux space for each participant (Talairach & Tournoux, 1988).

Whole brain analysis: Identification of regions of interest (ROIs)

Functional data were analysed using the general linear model (GLM). Experimental events (mean duration = 14.2 s) were convolved with a standard dual gamma haemodynamic response function. There were four regressors of interest (corresponding to the four experimental

conditions) and seven regressors of no interest, corresponding to the six motion correction parameters obtained during preprocessing and the response trials.

In order to identify the brain regions involved in the processing of uni- and bilaterally applied stimuli, group analysis (n = 17) was performed using a random-effects (RFX) GLM. Statistical maps were thresholded using a false discovery rate (FDR) (Genovese, Lazar & Nichols, 2002) of 0.05 and a cluster threshold of 4 voxels. ROIs were defined using a RFX contrast including only bilateral experimental conditions compared to baseline (i.e., [Ri-Li + Rm-Li] > Baseline). The baseline was estimated from all the periods in the time course that were not explicitly modelled in the design matrix. The rationale for including only bimanual stimulation conditions in the RFX contrast was that in our protocol, stimulation of the two fingers of both hands elicited the same level of activation in the two hemispheres. On the contrary, stimulation of the two fingers of the same hand did not elicit the same level of activation in both hemispheres, due to the primarily contralateral projection. Thus, excluding the unilateral conditions generates a functional map that reflects well-balanced activation of the two hemispheres. Note that this type of analysis, which includes only the bilateral stimulation conditions, has been performed only for identification of the ROIs.

In accordance with our hypothesis, ROIs of primary interest included the contra- and ipsilateral primary and secondary somatosensory cortices (cSI & cSII, iSI & iSII, respectively). Note that the terms "contralateral" and "ipsilateral" always refer to the side of the body to which the *adaptor* stimulus was applied. For instance, with bilateral homologous stimulation (i.e., right index and then left index fingers stimulated) cSI refers to the left SI. In addition to SI and SII, we defined other ROIs of secondary interest for completeness deriving from the activation maps. We predicted a modulation of activation in somatosensory areas (i.e., SI and SII) depending on the stimulation conditions. We defined ROIs on the basis of both functional and anatomical criteria (Dinstein, Gardner, Jazayeri, & Heeger, 2008; Cavina-Pratesi, Monaco, Fattori, Galletti,

McAdam, Quinlan, Goodale, & Culham, 2010; Gallivan, McLean, Valyear, Pettypiece, & Culham, 2011). A detailed description of the identification procedure for ROIs of primary interest is provided in the section 'Identification of SI and SII cortices and additional brain areas'.

Event-related averaging analysis

Event-related averaged responses of the four stimulation conditions were extracted for each ROI (i.e., cSI, cSII, iSI, iSII). For completeness, we also extracted the event-related averages from the other significantly active regions defined as ROIs of secondary interest (e.g., right inferior frontal gyrus (rIFG), bilateral thalamus (cT and iT), and posterior parietal cortex (PPC)). We computed the percent BOLD signal change with respect to the baseline, which was defined as the mean signal over the period between -2 and 0 s.

Considering that the average of the peak latencies for each condition differs depending on the ROI (i.e., difference in brain response between contralateral and ipsilateral tactile stimulation), we determined the peak latency of each of the four stimulation conditions and took the peak amplitude as an index of the event-related deconvolved BOLD response. For statistical analysis, peak amplitudes for all conditions were considered as dependent variables. In particular, the activation peak values of the percent BOLD signal change from the baseline were entered into two separate repeated measures ANOVAs: one for SI and one for SII, with HAND (within, between), HEMISPHERE (contralateral, ipsilateral) and FINGER (homologous, non-homologous) as within-participants factors. The Tukey HSD test was used for all post-hoc comparisons.

Results

Figure 3 shows the statistical map resulting from the t-contrast obtained when comparing the bilateral stimulation conditions against baseline, ("Ri-Li" + "Rm-Li") > ("baseline"), $t_{(16)} > 3.14$; $p < .0063$. Several clusters of activation were identified within the somatosensory cortices and in other regions of the brain (see next section), both in the right (Figure 3 a-c) and

the left (Figure 3 b-d) hemisphere. This statistical map served to compute all of the subsequent analyses, which include the event-related averaging of the defined ROIs. The results are organised in two sections: (1) identification of SI, SII and other vibrotactile responsive brain areas; (2) description of the fMRI adaptation effects.

< Please insert Figure 3 about here >

Identification of SI, SII and other vibrotactile responsive brain areas

SI localization. As shown in the functional activation map in Figure 3a-b, in both hemispheres the activated cluster of voxels within SI was quite large and spread into the PPC. The peak of activation of this large cluster of voxels (i.e., SI + PPC) was clearly located outside the anatomical SI region. However, visual inspection of the statistical map along the axial plane showed two clear segregated clusters of activation: one compatible with the anatomical location of SI and the other that included a wide portion of the PPC. To confirm the anatomical location of the presumed SI cluster, three approaches were used. First, we submitted the x, y, z-coordinates of the activation peak of the cluster to the Talairach Client software (http://www.talairach.org/; see Lancaster, Rainey, Summerlin, Freitas, Fox, Evans, Toga, & Mazziotta, 1997; Lancaster, Woldorff, Parsons, Liotti, Freitas, Rainey, Kochunov, Nickerson, Mikiten, & Fox, 2000), which labelled the coordinates as Brodmann's area 1 or 2. Second, we verified that the coordinates of the activation peak fell within the probabilistic map for SI obtained from a meta-analysis of fMRI data on 126 articles (see Mayka, Corcos, Leurgans, & Vaillacourt, 2006; Hlushchuk, & Hari, 2006; Nelson & Chen, 2008). Third, we checked the location of this functional activation against the structural images of various participants. As a resultant of these inspections, we selected a 3D volume of 10 x 10 x 10 mm around the identified peak as ROI for SI.

Notably, the location of SI in the two hemispheres was not completely symmetrical. SI was slightly more posterior in the left as compared to the right hemisphere. Although this activation resulted from stimulation occurring on both hands, it should be noted that in our protocol the left hand was stimulated more often and was constantly attended. Left SI was thus ipsilateral to this salient tactile stimulation. In this respect, this asymmetrical finding seems to parallel the results of recent work that detected ipsilateral SI activation using fMRI with unilateral medial nerve stimulation, and found that the position of this activation was located more posteriorly with respect to the homologous area in the contralateral hemisphere (Nihashi, Naganawa, Sato, Kawai, Nakamura, Fukatsu, Ishigaki, & Aoki, 2005).

Finally, we also identified the peak of the activation in PPC (see Figure 5) and compared its event-related averages with those extracted for SI.

SII localization. Similar to SI localization, the localization of SII was based on both functional and anatomical criteria (see Figure 2c-d). SII activation was well defined in space and clearly separated from other activation clusters. Therefore, we selected the peak of activation in those voxels identified by the RFX contrast located in the region of the operculum and defined a cube of 10 x 10 x 10 mm around this point. SII localization was, as for SI, checked with the Talairach Client software which confirmed that the selected region may be SII (see also Ploner, Schmitz, Freund, & Schnitzler, 2000).

Other active regions. In addition to the activations in somatosensory areas, a series of other brain areas showed a significant BOLD response to tactile stimulation (see Figure 3). These areas include the right IFG, the anterior cingulate cortex, bilateral thalamus, bilateral PPC (cPPC and iPPC), bilateral angular gyrus, bilateral supramarginal gyrus and bilateral inferior parietal lobule.

fMRI adaptation effect in the somatosensory cortices

Figure 4 shows the BOLD response in SI. Overall, BOLD response in SI was more pronounced for the contralateral (mean±SE = 0.645±0.16%) compared to the ipsilateral (mean±SE = 0.438±0.14%) hemisphere with respect to the adaptor stimulus (main effect of HEMISPHERE, $F(1,16) = 34.52$, $p < 0.0001$; see Figure 4). This is an expected finding and reflects the primarily contralateral response to tactile stimulation in SI (e.g., Nelson, & Chen, 2008; Overduin, & Servos, 2004; Ruben et al., 2001). Most importantly, the BOLD response was modulated as a function of which finger served as the adaptor, and which hemisphere was considered. As shown in Figure 4b, in the hemisphere contralateral to the adaptor, the BOLD response was reduced when the stimulation was delivered to the homologous (mean±SE = 0.574±0.11%) compared to the non-homologous fingers (mean±SE = 0.715±0.12%; $p < 0.0001$). This reduction was not significant in the hemisphere ipsilateral to the adaptor, resulting in a two-way interaction between HEMISPHERE and FINGER, $F(1,16) = 9.99$, $p < 0.006$. This shows a finger-specific adaptation that emerged selectively in SI contralateral to the adaptor.

Interestingly, there were no significant interactions involving the HAND factor. As can be noted from the visual comparison of bar plots for unilateral and bilateral stimulation (Figure 4b), the decreased BOLD response for the homologous in comparison to the non-homologous finger in the hemisphere contralateral to the adaptor was present for <u>both</u> unilateral and bilateral vibrotactile stimulation conditions. No other significant effects or interactions were found (all $ps > 0.08$), apart from a main effect of FINGER, $F(1,16) = 9.58$, $p < 0.007$, which was, however, subsidiary to the higher order interaction described above.

< Please insert Figure 4 and 5 about here >

Figure 5 shows the BOLD response in SII. Overall, unilateral stimulation (mean±SE = 0.600±0.04%) elicited a larger BOLD response in SII compared to bilateral stimulation (mean±SE = 0.470±0.05%; main effect of HAND, $F(1,16) = 98.83$, $p < 0.0001$). Figure 5b shows a general reduction in the BOLD response for the homologous (mean±SE = 0.505±0.09%) compared to the non-homologous fingers (mean±SE = 0.554±0.10%; main effect of FINGER, $F(1,16) = 7.83$, $p < 0.01$). This difference occurred regardless of whether the stimulation was unilateral or bilateral (as in SI), and was also equally present in both hemispheres (unlike in SI). No other significant effects or interactions were observed (all ps > 0.09).

BOLD response outside the somatosensory cortices

Outside the somatosensory cortices, only two vibrotactile responsive regions were modulated as a function of which finger was stimulated: the primary motor cortex (M1) and the right IFG (see Figure 6). In M1, an overall negative BOLD response was detected (INTERCEPT representing the baseline, $F(1,16) = 69.30$, $p < 0.0001$), and the ANOVA revealed a significant interaction between HEMISPHERE and FINGER, ($F(1,16) = 5.94$, $p < 0.03$). In M1 ipsilateral to the adaptor, negative BOLD response was smaller for homologous (mean±SE = -0.187±0.04%; p = 0.05 corrected) than non-homologous finger stimulation (mean±SE = -0.218±0.04%). By contrast, M1 contralateral to the adaptor showed no difference between homologous (mean±SE = -0.186±0.04%) and non-homologous stimulation (mean±SE = -0.179±0.04%; p = 0.93).

In the right IFG we ran two separate ANOVAs, one for each side of stimulation (i.e., within and between hands). This analysis revealed a greater BOLD response for the homologous (mean±SE = 0.339±0.05%) than non-homologous (mean±SE = 0.229±0.04%) finger when the stimulation was within the same hand (main effect of FINGER $F(1,16) = 21.68$, $p < 0.0003$), but

not when it was between the hands ($p > 0.3$). Note that in this brain region we found an increase rather than a decrease in the BOLD response for the homologous finger stimulation.

The analysis on the thalamus and PPC showed that these brain areas were not modulated as a function of finger. In particular, the ANOVA on the thalamus revealed a greater BOLD response for the contralateral (mean±SE = 0.286±0.08%) than ipsilateral (mean±SE = 0.265±0.07%) hemisphere with respect to the adaptor (main effect of HEMISPHERE, $F(1,16) = 11.37$, $p < 0.004$), the same was true also for the PPC (main effect of HEMISPHERE $F(1,16) = 8.45$, $p < 0.01$). Moreover, for the thalamus the BOLD response in the contralateral hemisphere was greater with unilateral (mean±SE = 0.327±0.06%) rather than bilateral (mean±SE = 0.246±0.05%; $p < 0.001$) fingers stimulation (interaction between HEMISPHERE and HAND $F(1,16) = 33.22$, $p < 0.0001$). No other significant effects or interactions were observed (all $p > 0.13$).

< Please insert Figure 6 about here >

Discussion

We used an fMRI adaptation approach to examine the contribution and bilateral interaction of SI and SII in the response to vibrotactile stimuli, delivered to fingers of same or different hands. Our results show that the overall BOLD response in SI was stronger in the hemisphere contralateral to the adaptor stimuli, whereas in SII it was equally distributed across the two hemispheres. This finding is consistent with the well-established fact that afferent inputs to SI are primarily contralateral, whereas in SII they are predominantly bilateral. Our fMRI adaptation approach, however, allowed acquiring finer grained insights into the nature of the representations contained in the somatosensory cortices. SI and SII adapted more strongly when the stimulation repeated over homologous than non-homologous fingers, thus showing that both these brain regions can clearly distinguish between the different fingers. Strikingly, our findings

also show that, in both somatosensory regions, this adaptation effect occur regardless of whether touches were delivered unilaterally or bilaterally. In other words, stronger adaptation to homologous than non-homologous finger stimulation emerged even when the touched fingers belonged to different hands. This result implies that both SI and SII can integrate ipsilateral and contralateral signals originating from the hands. No other tactually responsive area of the brain showed such a pattern of adaptation for homologous than non-homologous finger stimulation. This further indicates that the effects we observed in the somatosensory cortices are unlikely the result of modulations originating from other (earlier or later) stages of tactile stimulus processing. Instead, they most likely reflect the specific contribution of somatosensory cortices during tactile perception.

Adaptation effect in the somatosensory cortices

Adaptation effects in the somatosensory modality have been reported previously using fMRI. Li Hegner and colleagues (2007; see also Li Hegner et al., 2010) asked participants to discriminate two vibrotactile stimuli applied sequentially to the same finger (left middle fingertip). In half of the trials the same frequency was repeated twice, whereas in the remaining trials two different frequencies were used. Within the somatosensory cortices, fMRI adaptation emerged in SI contralaterally andin SII bilaterally. Our findings extend this result by showing that fMRI adaptation for tactile stimuli to the fingers can also emerge when the repeating feature of the stimulus is its spatial location (i.e., which finger was stimulated) rather than its frequency. In our study, adaptation emerged as a reduced BOLD response in homologous compared to non-homologous finger stimulation. Similar to Li Hegner et al. (2007), we found that this adaptation effect was lateralised in SI and bilateral in SII.

Our finger-specific adaptation effect was expected for the vibrotactile stimuli confined to a single hand (i.e., unilateral stimulation). Touches delivered twice to the same fingertip (unilateral homologous condition) stimulate the same region of skin and – to a large extent – the same

population of tactile receptors. By contrast, touches delivered to adjacent fingers (unilateral non-homologous condition) stimulate two distinct regions of skin and entirely different receptors. Thus, homologous finger stimulation likely activates the same population of neurons in the somatosensory cortex twice, whereas non-homologous finger stimulation activates populations of neurons that are – at best – partially overlapping in the somatosensory cortex (for evidence of partially overlapping cortical regions of the index and middle finger see Kurth, Villringer, Curio, Wolf, Krause, Repenthin, Schwiemann, Deuchert, & Villringer, 2000; Krause, Kurth, Ruben, Schwiemann, Villringer, Deuchert, Moosmann, Brandt, Wolf, Curioc, & Villringer, 2001).

Strikingly, stronger adaptation for homologous than non-homologous finger stimulation also emerged when the same stimuli were applied bilaterally. In this condition, no region of skin and no tactile receptors were shared between the two successive stimulations. The only common feature was the homology of body parts across sides (i.e., left and right *index* fingers). The present findings show that the only brain regions that were sensitive to this homology were the somatosensory cortices (both SI and SII), whereas no other brain region changed its BOLD response as a function of finger identity (with the notable exception of M1 and to some extent the rIFG, see below). When considered in terms of neural coding, this finding implies the existence of neural populations in both SI and SII that code for finger identity irrespective of side. While this notion is compatible with the existence of bilateral afferents and bilateral receptive fields in SII, it is more intriguing when considered within the well-known prevalence of contralateral afferents and contralateral receptive fields in SI.

Bilateral representations of the body in SI and SII

Evidence for contralateral responses in SI and more bilateral responses in SII is present also in our findings. As noted above, we found larger BOLD responses in the SI contralateral to the adaptor stimuli, but a more balanced bilateral BOLD response across the two hemispheres in

SII. Furthermore, our finger-specific adaptation effects were limited to the contralateral hemisphere in SI, but were bilateral in SII. This is also in line with the magnetoencephalographic (MEG) literature on tactile perception, which shows a primarily contralateral response in SI and a bilateral response in SII when adopting the classical approach of median nerve stimulation (e.g., Hari et al., 1993; Maldjian et al., 1999). Bilateral representations of the two sides of the body in SII (e.g., Hari, Karhu, Hämäläinen, Knuutila, Salonen, Sams, & Vilkman, 1993) are ascribed to more dense bilateral afferent inputs in SII in comparison to SI (e.g., Forss, Jousmäki, & Hari, 1995; Lin, & Forss, 2002; Maldjian, Gottschalk, Patel, Pincus, Detre, & Alsop, 1999).

However, neurophysiological studies in monkeys and neuroimaging studies in humans have now pointed out that neural representations of the body in SI are probably not only contralateral. Bilateral receptive fields have been found in the monkey somatosensory area 2 (Iwamura et al., 2001; Iwamura et al., 2002). Moreover, when stimuli were presented to both paws, interhemispheric interactions have been revealed in area 3b of the primary somatosensory cortex of owl monkeys (Reed, Qi, Zhou, Bernard, Burish, Bonds, and Kaas, 2010; Reed, Qi, & Kaas, 2011). In rats it has been demonstrated that SI is able to integrate inputs from the contralateral and ipsilateral whisker pads (Shuler, Krupa, & Nicolelis, 2001). In particular, Shuler and colleagues (2001) found that the neuronal responses in SI of one hemisphere (e.g., contralateral) after whisker pad stimulation were affected by a previous stimulus that reached the other hemisphere (e.g., ipsilateral). This effect was modulated as a function of the spatial location and the relative timing at which the whisker stimuli were presented. In humans, SI responses ipsilateral to a tactile stimulus have been shown using neuroimaging (Hlushchuk, & Hari, 2006; Staines, Graham, Black, & McIlroy, 2002). In addition, bilateral BOLD responses in both SI and SII have been recorded under unilateral sensory stimulation conditions (Blatow, Nenning, Durst, Sartor, & Stippich, 2007). Finally, behavioural studies in humans have corroborated these

observations by showing that tactile representations may not fully differentiate between body sides (Braun et al., 2005; Harris et al., 2001; Tamè et al., 2011).

Interactions between ipsilateral and contralateral inputs in SI may derive from different anatomical pathways, which are not mutually exclusive (Sutherland, 2006). One first possibility is that ipsilateral somatosensory inputs are conveyed transcallosally from the contralateral SI (Allison, McCarthy, Wood, Williamson, & Spencer, 1989). In rats, for instance, the pharmacological inactivation of SI in one hemisphere using muscimol eliminates the ipsilaterally-evoked whisker responses in the unaffected SI in the other hemisphere (Shuler, Krupa, & Nicolelis, 2001), supporting the hypothesis of information exchange between SI in the two hemispheres. A second possibility is the existence of direct projections from the receptor surface to ipsilateral SI (Kanno, Nakasato, Hatanaka, & Yoshimoto, 2003; Kanno et al., 2004), mediated by uncrossed afferent fibres (Kanno et al., 2003; Noachtar, Lüders, Dinner, & Klem, 1997). An MEG study on two patients with left hemispheric lesions found ipsilateral activation of the right SI after stimulation of the medial nerve of the right arm, despite impaired somatosensory responses in the left hemisphere (Kanno et al., 2003). This clinical finding potentially obviates the need for transcallosal pathways for the ipsilateral activation of SI. Finally, cortico-cortical modulations of SI could also emerge via transcallosal connections between homotopic SII regions (Schnitzler, Salmelin, Salenius, Jousmäki, & Hari, 1995; Tommerdahl et al., 2006).

The low temporal resolution of fMRI does not allow us to determine the time course of the interaction between contralateral and ipsilateral tactile stimulation in SI and SII, thus preventing any definite conclusion about the pathway leading to the interactions between ipsilateral and contralateral signals observed here in SI. Interestingly, our data showed a trend towards a delayed activation peak of the overall BOLD response in the ipsilateral compared to the contralateral SI. This trend may have failed to reach significance due to the adopted TR (2.2 s), which does not provide sufficient temporal precision to characterise this temporal difference.

It would be relevant to assess this pattern in a dedicated study, as this could speak in favour of a transcallosal interaction from SII to ipsilateral SI. In this respect, preliminary evidence we collected with MEG, using a similar paradigm to the one described here, suggest that transcallosal interactions may be more likely than direct ipsilateral afferent projections (Braun, Tamè, Papadelis, Farnè, & Pavani, 2011). Particularly, transcallosal interactions at the level of SII are also possible due to its strong anatomical connections with SI (Caminiti, Innocenti, & Manzoni, 1979; Manzoni, Conti & Fabri, 1986) implying a quite local top-down modulation within the somatosensory cortex. As noted by Shuler et al. (2001), ipsilateral evoked activity in primary sensory cortices has been largely accounted for by transcallosal pathways in other sensory systems and species (e.g., Berlucchi et al., 1967; Swadlow, 1974; Manzoni et al., 1989; Schnitzler et al., 1995; Iwamura et al., 2001). Whatever the particular pathway the tactile inputs travel to join ipsilateral SI, the present study indicated that integration of inputs from the two body sides can occur in SI as well as in SII.

Adaptation effect outside of the somatosensory cortex

Outside somatosensory regions, none of the vibrotactually responsive brain areas showed specific adaptation for homologous in comparison to non-homologous fingers. The fact that the adaptation pattern does not come from the previous stages (e.g., thalamus) nor propagate to further stages (e.g., PPC) of the tactile processing suggests that the distinction between fingers and the interaction between body sides occurs within the somatosensory cortex.

The only two exceptions were the right IFG and M1. The rIFG showed an increased BOLD response when the target finger was stimulated twice (i.e., left index twice) compared to when non-homologous finger of the same hand was stimulated (i.e., left middle and left index). rIFG is a well known region of the brain network activated during stimulus-driven attentional orienting (e.g., Corbetta, & Shulman, 2002). Thus, this effect is likely attributable to attentional

cueing to the test finger, when the preceding stimulation occurred exactly in the same location. More relevant to the purpose of the present study, and directly related to the adaptation effects examined for the somatosensory cortices, is the modulation of BOLD response we found in the M1 ipsilateral to the adaptor. M1 showed a general deactivation pattern for all stimulation conditions. Previous studies in humans reported inhibition of M1 during sensory-motor interactions (e.g., Tokimura, Di Lazzaro, Tokimura, Oliviero, Profice, Insola, Mazzone, Tonali, & Rothwell, 2000; Bikmullina, Kičić, Carlson, & Nikulin, 2009). Furthermore, studies in conscious monkeys showed that many neurons in the primary motor cortex respond to cutaneous stimulation (e.g., Lemon, 1981), and that Brodmann's areas 1 and 2 are strongly anatomically connected with M1 (Stepniewska, Preuss, & Kaas, 2004). The deactivation pattern we revealed in left M1 was exactly mirror symmetric to the finger-specific adaptation effect we reported in somatosensory cortices. This suggests a very close and low-level inhibitory interaction between the somatosensory and motor cortices, indicating that the study of M1 can be informative about the representation of touch in somatosensory regions, and particularly SI. It is unclear why the effect in M1 was only present in the hemisphere ipsilateral to the adaptor. However, one previous study on a patient with Klippel-Feil syndrome and mirror movements of the hand muscles (Farmer et al., 1990) reported that digital nerve stimulation produced an inhibitory response only in the muscles ipsilateral to the stimulus, meaning that low level interactions between the somatosensory and the motor cortices of opposite hemispheres are possible.

Conclusions

Using fMRI adaptation to study the spatial coding of touch, the present work shows that the primary somatosensory cortex can homotopically integrate somatosensory inputs from the two sides of the body, despite its prominent contralateral response. This finding extends the contribution of SI to spatial coding of touch beyond the mere distinction of body parts (i.e.,

somatotopy). The involvement of SI in the processing of somatosensory stimuli from both sides of the body is in accordance with a growing body of evidence in animals and humans that suggest that SI can be "an actual site of integration, rather than merely a conduit for sensory information that is integrated at higher processing stages" (Shuler et al., 2001, p.2967). As such, it may play a role in the integration of bilateral somatosensory input required, for instance, during bimanual exploration of objects.

Acknowledgements

We are grateful to Dr. Francesco Prantil for the conditions randomization program and Dr. Nicholas P Holmes for comments on the manuscript. This work has been realized also thanks to the support from the Provincia Autonoma di Trento and the Fondazione Cassa di Risparmio di Trento e Rovereto. A.F. was supported by the ANR grant No. RPV08085CSA and the James S. McDonnell Scholar Award.

References

Allison, T., McCarthy, G., Wood, C. C., Williamson, P. D., & Spencer, D. D. (1989). Human cortical potentials evoked by stimulation of the median nerve. II. Cytoarchitectonic areas generating long-latency activity. *Journal of Neurophysiology,* 62, 711-22.

Berlucchi, G., Gazzaniga, M. S., Rizzolatti, G. (1967). Microelectrode analysis of transfer of visual information by the corpus callosum. *Arch Ital Biol,* 105, 583–596.

Blatow, M., Nennig, E., Durst, A., Sartor, K., & Stippich, C. (2007). fMRI reflects functional connectivity of human somatosensory cortex. *Neuroimage*, 37, 927-936.

Bikmullina, R., Kičić, D., Carlson, S., & Nikulin, V. V. (2009). Electrophysiological correlates of short-latency afferent inhibition: a combined EEG and TMS study. *Experimental Brain Research*, 194, 517-526.

Braun, C., Tamè, L., Papadelis, C., Farnè, A., Pavani, F. (2011). Multiple representations of touch. *11th International Conference on Cognitive Neuroscience* (ICON XI), Mallorca, Spain, 25-29 September.

Braun, C., Hess, H., Burkhardt, M., Wühle, A., & Preissl, H. (2005). The right hand knows what the left hand is feeling. *Experimental Brain Research,* 162, 366–373.

Brozzoli, C., Gentile, G., Petkova, V. I., & Ehrsson, H. H. (2011). fMRI adaptation reveals a cortical mechanism for the coding of space near the hand. *Journal of Neuroscience*, 31(24), 9023-9031.

Bush, G., Vogt, B. A., Holmes, J., Dale, A. M., Greve, D., Jenike, M. A., & Rosen, B. R. (2002). Dorsal anterior cingulate cortex: A role in reward-based decision making. *PNAS*, 99, 523-528.

Caminiti, R., Innocenti, G. M., & Manzoni, T. (1979). The anatomical substrate of callosal messages from SI and SII in the cat. *Experimental Brain Research*, 35(2), 295-314.

Cavina-Pratesi, C., Monaco, S., Fattori, P., Galletti, C., McAdam, T. D., Quinlan, D. J., Goodale, M. A., & Culham, J. C. (2010). Functional magnetic resonance imaging reveals the neural substrates of arm transport and grip formation in reach-to-grasp actions in humans. *Journal of Neuroscience*, 30(31), 10306-10323.

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Review Neuroscience*, 3(3), 201-215.

Del Gratta, C., Della Penna, S., Ferretti, A., Franciotti, R., Pizzella, V., Tartaro, A., Torquati, K., Bonomo, L., Romani, G. L, & Rossini, P. M. (2002). Topographic Organization of the Human Primary and Secondary Somatosensory Cortices: Comparison of fMRI and MEG Findings. *Neuroimage*, 17, 1373-1383.

Dinstein, I., Gardner, J. L., Jazayeri, M., & Heeger, D. J. (2008). Executed and observed movements have different distributed representations in human aIPS. *Journal of Neuroscience*, 28(44), 11231-11239.

Farmer, S. F., Ingram, D. A., & Stephens, J. A. (1990). Mirror movements studied in a patient with KlippelFeil syndrome. *Journal of Physiology,* 428, 467-484.

Forss, N., Jousmäki, V., Hari, R. (1995). Interaction between afferent input from fingers in human somatosensory cortex. *Brain Research*, 685, 68-76.

Francis, S. T., Kelly, E. F., Bowtell, R., Dunseath, W. J. R., Folger, S. E., & McGlone, F. (2000). fMRI of the responses to vibratory stimulation of digit tips. *Neuroimage*, 11, 188-202.

Friedman, D., Jones, E., & Burton, H. (1980). Representation pattern in the second somatic sensory area of the monkey cerebral cortex. *Journal of Comparative Neurology*, 192, 1021-1041.

Fritsch, G., & Hitzig, D. (1870). On the electrical excitability of the cerebrum In: Von Bonin G (1960) trans., Some Papers on the Cerebral Cortex. Springfield IL, Charles C. Thomas.

Gallivan, J. P., McLean, D. A., Valyear, K. F., Pettypiece, C. E., & Culham, J. C. (2011). Decoding action intentions from preparatory brain activity in human parieto-frontal networks. *Journal of Neuroscience*, 31(26), 9599-9610.

Genovese, C. R., Lazar, N. A., & Nichols, T. (2002). Thresholding of statistical maps in functional neuroimaging using the false discovery rate. *Neuroimage*, 15(4), 870-878.

Grill-Spector, K., & Malach, R. (2001). fMRI-adaptation: A tool for studying the functional properties of human cortical neurons. *Acta Psychologica (Amst),* 101(1-3), 293-321.

Gross, C. G., Rocha-Miranda, C. E., & Bender, D. B. (1972). Visual properties of neurons in inferotemporal cortex of the macaque. *Journal of Neurophysiology*, 35, 96–111.

Hari, R., Karhu, J., Hämäläinen, M., Knuutila, J., Salonen, O., Sams, M., & Vilkman, V. (1993). Functional organization of the human first and second somatosensory cortices: a neuromagnetic study. *European Journal of Neuroscience*, 5(6), 724-734.

Harris, J. A., Harris, I. M., & Diamond, M. E. (2001). The topography of tactile working memory. *Journal of Neuroscience,* 21, 8262–8269.

Hlushchuk, Y., & Hari, R. (2006). Transient suppression of ipsilateral primary somatosensory cortex during tactile finger stimulation. *Journal of Neuroscience*, 26(21), 5819-5824.

Iwamura, Y., Taoka, M., & Iriki, A. (2001). Bilateral activity and callosal connections in the somatosensory cortex. *The Neuroscientist*, 7, 419–429.

Iwamura, Y., Tanaka, M., Iriki, A., Taoka, M., & Toda, T. (2002). Processing of tactile and kinesthetic signals from bilateral sides of the body in the postcentral gyrus of awake monkeys. *Behavioural Brain Research*, 135, 185–190.

Kanno, A., Nakasato, N., Hatanaka, K., & Yoshimoto, T. (2003). Ipsilateral area 3b responses to median nerve somatosensory stimulation. *NeuroImage,* 18, 169-77.

Kanno, A., Nakasato, N., Nagamine, Y., & Tominaga, T. (2004). Non-transcallosal ipsilateral area 3b responses to median nerve stimulus. *Journal of Clinical Neuroscience,* 11, 868-71.

Kawashima, R., Satoh, K., Itoh, H., Ono, S., Furumoto, S., Gotoh, R., Koyama, M., Yoshioka, S., Takahashi, T., Takahashi, K., Yanagisawa, T., & Fukuda, H. (1996). Functional anatomy of GO/NO-GO discrimination and response selection -a PET study in man. *Brain Research,* 728, 79-89.

Killackey, H. P., Gould, H. J. III., Cusick, C. G., Pons, T. P., & Kaas, J. H. (1983). The relation of corpus callosum connections to architectonic fields and body surface maps in sensorimotor cortex of New and Old World monkeys. *Journal of Comparative Neurology*, 219, 384–419.

Korvenoja, A., Huttunen, J., Salli, E., Pohjonen, H., Martinkauppi, S., Palva, J. M., Lauronen, L., Virtanen, J., Ilmoniemi, R. J., & Aronen, H. J. (1999). Activation of multiple cortical areas in response to somatosensory stimulation: combined magnetoencephalographic and functional magnetic resonance imaging. *Human Brain Mapping*, 8, 13-27.

Kourtzi, Z., & Kanwisher, N. (2000). Cortical regions involved in perceiving object shape. *Journal of Neuroscience*, 20(9), 3310-3318.

Krause, T., Kurth, R., Ruben, J., Schwiemann, J., Villringer, K., Deuchert, M., Moosmann, M., Brandt, S., Wolf, K. J., Curioc, G., & Villringer, A. (2001). Representational overlap of adjacent fingers in multiple areas of human primary somatosensory cortex depends on electrical stimulus intensity: an fMRI study. *Brain Research*, 899, 36-46.

Krekelberg, B., Boynton, G. M., & van Wezel, R. J. A. (2006). Adaptation: from single cells to BOLD signals. *Trends in Neuroscience*, 29(5), May.

Kurth, R., Villringer, K., Curio, G., Wolf, K. J., Krause, T., Repenthin, J., Schwiemann, J., Deuchert, M., & Villringer, A. (2000). fMRI shows multiple somatotopic digit representations in human primary somatosensory cortex. *Neuroreport*, 11, 1487-1491.

Lancaster, J. L., Rainey, L. H., Summerlin, J. L., Freitas, C. S., Fox, P. T., Evans, A. C., Toga, A. W., & Mazziotta, J. C. (1997). Automated labeling of the human brain: a preliminary report

on the development and evaluation of a forward-transform method. *Human Brain Mapping*, 5, 238-242.

Lancaster, J. L., Woldorff, M. G., Parsons, L. M., Liotti, M., Freitas, C. S., Rainey, L., Kochunov, P. V., Nickerson, D., Mikiten, S. A., & Fox, P. T. (2000). Automated talairach atlas labels for functional brain mapping. *Human Brain Mapping*, 10, 120-131.

Lemon, R. N. (1981). Functional properties of monkey motor cortex neurones receiving afferent input from the hand and fingers. *The Journal of Physiology*, 311, 497-519.

Lingnau, A., Ashida, H., Wall, M. B., & Smith, A. T. (2009). Speed encoding in human visual cortex revealed by fMRI adaptation. *Journal of Vision*, 9(13), 3. 1-14.

Li Hegner, Y., Saur, R., Veit, R., Butts, R., Leiberg, S., Grodd, W., & Braun, C. (2007). BOLD adaptation in vibrotactile stimulation: neural networks involved in frequency discrimination. *Journal of Neurophysiology*, 97, 264-271.

Li Hegner, Y., Lee, Y., Grodd, W., & Braun, C. (2010). Comparing tactile pattern and vibrotactile frequency discrimination: a human FMRI study. *Journal of Neurophysiology*, 103(6), 3115-3122.

Lin, Y. Y., & Forss, N. (2002). Functional characterization of human second somatosensory cortex by magnetoencephalography. *Behavioural Brain Research*, 135, 141-145.

Maldjian, J. A., Gottschalk, A., Patel, R. S., Detre, J. A., & Alsop, C. (1999). The sensory somatotopic map of the human hand demonstrated at 4 Tesla. *Neuroimage*, 10, 55-62.

Manzoni, T., Barbaresi, P., Conti, F., & Fabri, M. (1989). The callosal connections of the primary somatosensory cortex and the neural bases of midline fusion. *Experimental Brain Research,* 76, 251–266.

Manzoni, T., Conti, F., & Fabri, M. (1986). Callosal projections from area SII to SI in monkeys: Anatomical organization and comparison with association projections. *Journal of Comparative Neurology*, 252(2), 245-263.

Mayka, M. A., Corcos, D. M., Leurgans, S. E., & Vaillancourt, D. E. (2006). Three-dimensional locations and boundaries of motor and premotor cortices as defined by functional brain imaging: A meta-analysis. *Neuroimage*, 31, 1453-1474.

Nelson, A. J., & Chen, R. (2008). Digit somatotopy within cortical areas of the postcentral gyrus in humans. *Cerebral Cortex*, 18, 2341-2351.

Nihashi, T., Naganawa, S., Sato, C., Kawai, H., Nakamura, T., Fukatsu, H., Ishigaki, T., & Aoki, I. (2005). Contralateral and ipsilateral responses in primary somatosensory cortex following electrical median nerve stimulation – an fMRI study. *Clinical Neurophysiology*, 116, 842-848.

Noachtar, S., Lüders, H. O., Dinner, D. S., & Klem, G. (1997). Ipsilateral median somatosensory evoked potentials recorded from human somatosensory cortex. *Electroencephalography Clinical Neurophysiology,* 104, 189-98.

Overduin, S. A., & Servos, P. (2004). Distributed digit somatotopy in primary somatosensory cortex. *Neuroimage*, 23, 462-472.

Penfield, W., & Rasmussen, T. (1950). The cerebral cortex of man; a clinical study of localization of function, Macmillan, New York.

Ploner, M., Schmitz, F., Freund, H. J., & Schnitzler, A. (2000). Differential organization of touch and pain in human primary somatosensory cortex. *Journal of Neurophysiology*, 83, 1770-1776.

Pons, T., Garraghty, P., & Mishkin, M. (1988). Lesion-induced plasticity in the second somatosensory cortex. *PNAS*, USA, 85, 5279-5281.

Reed, J. L., Qi, H. X., Zhou, Z., Bernard, M. R., Burish, M. J., Bonds, A. B., & Kaas, J. H. (2010). Response properties of neurons in primary somatosensory cortex of owl monkeys reflect widespread spatiotemporal integration. *Journal of Neurophysiology*, 103, 2139-2157.

Reed, J. L., Qi, H. X., & Kaas, J. H. (2011). Spatiotemporal properties of neuron response suppression in owl monkey primary somatosensory cortex when stimuli are presented to both hands. *Journal of Neuroscience*, 31(10), 3589-3601.

Ruben, J., Schwiemmann, J., Deuchert, M., Meyer, R., Krause, T., Curio, G., Villringer, K., Kurth, R., & Villringer, A. (2001). Somatotopic organization of human secondary somatosensory cortex. *Cerebral Cortex*, 11, 463-473.

Sanchez-Panchuelo, R. M., Francis, S., Bowtell, R., & Schluppeck, D. (2010). Mapping human somatosensory cortex in individual subjects with 7T functional MRI. *Journal of Neurophysiology*, 103, 2544-2556.

Schnitzler, A., Salmelin, R., Salenius, S., Jousmäki, V., & Hari, R. (1995). Tactile information from the human hand reaches the ipsilateral primary somatosensory cortex. *Neuroscience Letters,* 200, 25-8.

Schwarzbach, J. V. (in press). A Simple Framework (ASF) for behavioural and neuroimaging experiments based on the Psychophysics Toolbox for Matlab. *Behavioural Research Methods.*

Schweizer, R., Braun, C., Fromm, C., Wilms, A., & Birbaumer, N. (2001). The distribution of mislocalizations across fingers demonstrates training-induced neuroplastic changes in somatosensory cortex. *Experimental Brain Research,* 139, 435–442.

Shmuel, A., Yacoub, E., Pfeuffer, J., Van de Moortele, P.F., Adriany, G., Hu, X., & Ugurbil, K. (2002). Sustained negative BOLD, blood flow and oxygen consumption response and its coupling to the positive response in the human brain. *Neuron*, 36, 1195-1210.

Shuler, G. M., Krupa, D. J., & Nicolelis, M. A. L. (2001). Bilateral integration of whisker information in the primary somatosensory cortex of rats. *Journal of Neuroscience*, 21(14), 5251-5261.

Staines, W. R., Graham, S. J., Black, S. E., & McIlroy, W. E. (2002). Task-relevant modulation of contralateral and ipsilateral primary somatosensory cortex and the role of a prefrontal-cortical sensory gating system. *NeuroImage*, 15, 190–199.

Stepniewska, I., Preuss, T. M., & Kaas, J. H. (1993). Architectionis, somatotopic organization, and ipsilateral cortical connections of the primary motor area (M1) of owl monkeys. *The Journal of Comparative Neurology*, 330, 238-271.

Sutherland, M. T. (2006). The hand and the ipsilateral primary somatosensory cortex. *Journal of Neuroscience*, 26(32), 8217-8218.

Swadlow, H. A. (1990). Efferent neurons and suspected interneurons in S-1 forelimb representation of the awake rabbit: receptive fields and axonal properties. *Journal of Neurophysiology*, 63,1477–1498.

Talairach, J., & Tournaux, P. (1988). Co-Planar Stereotaxic Atlas of the Human Brain (Thieme, New York).

Tamè, L., Farnè, A., & Pavani, F. (2011). Spatial coding of touch at the fingers: Insights from double simultaneous stimulation within and between hands. *Neuroscience Letters*, 487, 78-82.

Tanaka, K., Saito, H. A., Fukada, Y., & Moriya, M. (1991). Coding visual images of objects in the inferotemporal cortex of the macaque monkey. *Journal of Neurophysiology*, 66, 170–189.

Tokimura, H., Di Lazzaro, V., Tokimura, Y., Oliviero, A., Profice, P., Insola, A., Mazzone, P., Tonali, P., & Rothwell, J. C. (2000). Short latency inhibition of human hand motor cortex by somatosensory input from the hand. *Journal of Physiology*, 523, 503-513.

Tommerdahl, M., Simons, S. B., Chiu, J. S., Favorov, O., & Whitsel, B. L. (2006). Ipsilateral input modifies the primary somatosensory cortex response to contralateral skin flutter. *Journal of Neuroscience,* 26, 5970-7.

Vuilleumier, P., Henson, R. N. A., Driver, J., & Dolan, R. J. (2002). Multiple levels of visual object constancy revealed by event-related fMRI of repetition priming. *Nature Neuroscience*, 5(5), 491-499.