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EFFECTIVE CONNECTIVITY DURING HAPTIC PERCEPTION: A STUDY USING GRANGER CAUSALITY ANALYSIS OF FUNCTIONAL MAGNETIC RESONANCE IMAGING DATA

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Abstract

Although it is accepted that visual cortical areas are recruited during touch, it remains uncertain whether this depends on top-down inputs mediating visual imagery or engagement of modality-independent representations by bottom-up somatosensory inputs. Here we addressed this by examining effective connectivity in humans during haptic perception of shape and texture with the right hand. Multivariate Granger causality analysis of functional magnetic resonance imaging (fMRI) data was conducted on a network of regions that were shape- or texture-selective. A novel network reduction procedure was employed to eliminate connections that did not contribute significantly to overall connectivity. Effective connectivity during haptic perception was found to involve a variety of interactions between areas generally regarded as somatosensory, multisensory, visual and motor, emphasizing flexible cooperation between different brain regions rather than rigid functional separation. The left postcentral sulcus (PCS), left precentral gyrus and right posterior insula were important sources of connections in the network. Bottom-up somatosensory inputs from the left PCS and right posterior insula fed into visual cortical areas, both the shape-selective right lateral occipital complex (LOC) and the texture-selective right medial occipital cortex (probable V2). In addition, top-down inputs from left postero-supero-medial parietal cortex influenced the right LOC. Thus, there is strong evidence for the bottom-up somatosensory inputs predicted by models of visual cortical areas as multisensory processors and suggestive evidence for top-down parietal (but not prefrontal) inputs that could mediate visual imagery. This is consistent with modality-independent representations accessible through both bottom-up sensory inputs and top-down processes such as visual imagery.

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INTRODUCTION

It is now firmly established that human tactile perception routinely evokes activity in visual cortical areas (reviewed by Sathian and Lacey, 2007). However, the mechanisms underlying such cross-modal recruitment of visual cortex remain uncertain. One idea is that visual imagery could be responsible (Sathian et al., 1997; Sathian & Zangaladze, 2001; Stoesz et al., 2003; Zangaladze et al., 1999; Zhang et al., 2004), whereas other work argues in favor of a common multisensory representation that is engaged by both visual and tactile processing (Amedi et al., 2001, 2002; James et al., 2002; Lacey et al., 2007). The visual imagery explanation implies involvement of top-down connections from prefrontal or posterior parietal cortex into visual cortical areas (Mechelli et al., 2004), while a multisensory representation might be derived from bottom-up tactile inputs into “visual” cortical areas. Examining the connectivity of the active areas could therefore help to distinguish between these possibilities. Two types of connectivity analysis are commonly distinguished: effective connectivity analysis involves estimation of the direction and strength of connections between regions of interest (ROIs), whereas functional connectivity analysis relies on discerning correlations between activity in various ROIs (Büchel and Friston, 2001).

In an earlier report (Peltier et al., 2007), we examined the effective connectivity of parietal and occipital cortical regions during haptic shape perception, using exploratory structural equation modeling (ESEM). ESEM was introduced to allow examination of connectivity without *a priori* assumptions about the underlying model (Zhuang et al., 2005). However, owing to the computational limitations imposed by the exponential increase in the number of possible models to be tested as the number of ROIs is increased in ESEM, we had to limit analysis to five ROIs. We chose in this earlier report (Peltier et al., 2007) to focus on a subset of parietal and occipital shape-selective areas active during haptic perception, out of a larger set of shape- and texture-selective areas identified in a functional magnetic resonance imaging (fMRI) study, the activation data from which have been published separately (Stilla and Sathian, 2007). The ESEM analysis revealed the existence of bidirectional information flow between parietal and occipital areas, suggesting that both bottom-up and top-down paths might be present. In the present report, we expanded the scope of effective connectivity analysis by including all 25 significantly activated ROIs from the study of Stilla and Sathian (2007), both shape- and texture-selective, using a different approach, analysis of Granger causality.

Granger causality is based on the principle of temporal predictability (Granger, 1969). Accordingly, increased predictability of the future temporal evolution of activity in one region of interest, ROI-1, from knowledge of the past temporal evolution of activity in another ROI, ROI-2, would imply that the ROI-2 time series “Granger causes” the ROI-1 time series. This basic concept has been utilized in formulating bivariate (Roebroeck et al., 2005; Abler et al., 2006) and multivariate Granger causality models (Kus et al., 2004; Deshpande et al., 2007; Stilla et al., 2007) which have been successfully applied to electrophysiological data (Ding et al., 2000; Kaminski et al., 2001; Korzeniewska et al., 2003; Kus et al., 2004; Blinowska et al., 2004) as well as fMRI data measuring the blood oxygenation-level dependent (BOLD) response (Roebroeck et al., 2005; Abler et al., 2006; Deshpande et al., 2007; Stilla et al., 2007). In the present study, we employed a multivariate Granger causality model (Kus et al., 2004; Deshpande et al., 2007; Stilla et al., 2007) capable of capturing simultaneous directional interactions between a large number of ROIs (25 ROIs in this study) in a computationally tractable manner. While such a model allows us to obtain effective connectivity networks from a large number of ROIs without any *a priori* assumptions about the underlying model, interpreting the resulting network could be quite challenging. Therefore, we introduce a principled way of reducing the size of the network by eliminating ROIs which do not contribute significantly to overall network connectivity. This approach allowed us to consider all

significantly activated ROIs in the initial stage of analysis while narrowing interpretation to the most significant ROIs in the later stage.

The primary aim of the present study was to use multivariate Granger causality analysis of effective connectivity to test two alternative, but not necessarily mutually exclusive hypotheses to explain cross-modal visual cortical recruitment during touch: (1) that haptic perception is associated with top-down inputs from prefrontal and/or posterior parietal cortex to visual cortex, offering a potential substrate for visual imagery mediation, and (2) that haptic perception is associated with bottom-up inputs from somatosensory to visual cortex, providing a potential substrate for haptic recruitment of a multisensory representation housed in “visual” cortex. A secondary aim was to refine available methods for multivariate Granger causality analysis to allow execution of the primary aim.

METHODS

MR imaging of haptic perception

Full details of subjects, stimulation, image acquisition and analysis can be found in the published report of haptic shape- and texture-selectivity (Stilla and Sathian, 2007); only a brief summary is given here. All procedures were approved by the Institutional Review Board of Emory University. The study was performed, with informed consent, on six neurologically normal, right-handed subjects (3 males and 3 females, mean age 22 years, age range 19–24 years). MR scans were performed on a 3 Tesla Siemens Trio whole body scanner (Siemens Medical Solutions, Malvern, PA), using a standard quadrature headcoil. Functional images with BOLD contrast were acquired using a T2*-weighted single-shot gradient-recalled echoplanar imaging (EPI) sequence comprising axial 5 mm-thick slices with full-brain coverage and the following parameters: repetition time (TR) 2000 ms, echo time 30 ms, flip angle 90°, in-plane resolution 3.4×3.4 mm, and in-plane matrix 64×64. High-resolution 3D anatomic images were also acquired.

Haptic stimulation runs consisted of interleaved blocks of shape and texture discrimination; separate visual stimulation runs were also conducted but they are not considered in the present report. The haptic shapes (HS) were 3D meaningless objects with identical texture and approximately the same size, but varying shape. The haptic textures (HT) were produced by adhering textured fabric or upholstery onto cardboard substrates of identical shape and size. In each haptic trial, an experimenter placed stimuli in the subject's right hand for 5 s, with a 1 s inter-stimulus interval. The stimuli were presented in a fixed orientation, and subjects were instructed not to rotate or re-orient objects during exploration. In the inter-stimulus intervals, the subject pressed one of two buttons on a fiberoptic response box, with the second or third digit of the left hand, to indicate whether the stimulus was identical to or different from the immediately preceding stimulus. Each type of stimulation block was repeated six times in a run. Trials and blocks were presented in different, pseudorandomized orders for each subject. Subjects were never allowed to see the haptic stimuli; their eyes were closed during haptic exploration in order to avoid visual stimulation and distraction, and to minimize eye movements. Presentation software (Neurobehavioral Systems, Albany, CA) was used to control stimulus timing and record responses.

Image processing and analysis was performed using BrainVoyager QX v1.6.1 (Brain Innovation, Maastricht, The Netherlands). For each subject, the functional images were realigned to the first image of the series; pre-processed utilizing trilinear interpolation for motion correction, sinc interpolation for slice scan time correction, and high-pass temporal filtering to 1 Hz; co-registered to the anatomic images; and transformed into Talairach space (Talairach and Tournoux, 1988). For group analysis, the transformed data were spatially smoothed with an isotropic Gaussian kernel (full width half maximum = 4mm), and baseline

periods were z-normalized. Statistical analysis of group data used random-effects, general linear models (GLM) followed by pairwise contrasts and correction for multiple comparisons within the cerebral cortical volume (corrected $p < 0.05$) by imposing a cluster-volume threshold for contiguous voxels that each passed a significance threshold of $p < 0.05$, using a 3D extension (implemented in BrainVoyager QX) of the 2D Monte Carlo simulation procedure described by Forman et al. (1995). Since many activated regions were confluent with one another, the thresholds were increased as necessary to resolve separable activations.

Connectivity analysis

Multivariate analysis of Granger causality—The approach is based on a multivariate vector autoregressive (MVAR) model capable of capturing the simultaneous directional influences between multiple ROIs. Kus and colleagues (2004) compared the performance of many estimators of multivariate Granger causality such as the directed transfer function (DTF), the direct DTF (dDTF) and partial directed coherence (PDC) and concluded that dDTF is effective for inferring direct influences. This is achieved by suppressing mediated influences using partial coherence (Kus et al., 2004). We have presented a variation of dDTF in our earlier applications to fMRI data (Deshpande et al., 2007; Stilla et al., 2007) wherein dDTF was not normalized so as to allow equitable comparison between connection strengths. Accordingly, letting $H_{ij}(f)$ and $\chi_{ij}(f)$ represent the non-normalized DTF and partial coherence, respectively, between ROIs i and j as defined by Kus et al (2004), we define dDTF as follows.

$$dDTF_{ij} = \sum_f H_{ij}(f) \chi_{ij}(f) \quad (1)$$

ROIs were created for each of a total of 25 activation sites from the HS – HT and HT – HS contrasts, centered on the activation maxima and constrained to be no larger than a $5 \times 5 \times 5$ mm cube. The entire time series of BOLD signal intensities from these ROIs, averaged across voxels within each ROI, were normalized across runs and subjects and concatenated across all runs and subjects to form a single vector per ROI. An MVAR model was fit to the resultant time series from the 25 ROIs and a dDTF connectivity matrix was obtained as outlined above. The statistical significance of the path weights thus obtained was ascertained using surrogate data (Theiler et al., 1992; Kaminski et al., 2001; Kus et al., 2004; Deshpande et al., 2007; Stilla et al., 2007). Surrogate data were generated by randomizing the phase of the original time series spectrum while retaining its magnitude. The dDTFs obtained from the surrogate data are expected to follow a null distribution since causal relations are destroyed by phase randomization. Thus, a null distribution was obtained by generating 2500 sets of surrogate data and calculating the dDTF (for every connection) from these 2500 datasets. The dDTF value obtained from the original time series was compared with the null distribution for a one-tailed test of significance with a p-value of 0.05.

Network Reduction—Even with the statistical thresholding, the 25-ROI connectivity matrix contains a huge number of connections and is difficult to interpret. Therefore, the network was further reduced by removing ROIs which did not significantly reduce the overall network connectivity upon their elimination. Identification of such ROIs was based on the principle of minimizing a cost function during the process of reduction. The cost function was designed to reflect the reduction of overall connectivity in the network. The procedure was as follows. Let the connectivity matrix of the original R ROIs be A . Upon removal of an ROI, a connectivity matrix B was determined using the remaining $R-1$ ROIs. The overall connectivity of A and B , designated as S_A and S_B , respectively, are given below where $N_R = R(R-1)$ are the total number of possible connections.

$$S_A = \frac{1}{N^R} \sum_{i=1}^R \sum_{j=1; i \neq j}^R A(i,j) \quad (2)$$

$$S_B = \frac{1}{N^{R-1}} \sum_{i=1}^{R-1} \sum_{j=1; i \neq j}^{R-1} B(i,j) \quad (3)$$

The cost function to be minimized is given as

$$\eta = S_A - S_B \quad (4)$$

If η was statistically insignificant, the ROI under consideration was considered not to have a significant contribution to the network and dropped. To determine the statistical significance of η , surrogate data were employed. A null distribution of η was obtained from surrogate time series (as described before) and compared to the value obtained from the original time series. The ROI under consideration was retained if η was found to be significantly positive ($p < 0.05$). The above procedure was started with 25 ROIs and iteratively applied by dropping the least significant ROI at each iteration, whereupon the network was recalculated with the remaining ROIs. The procedure was terminated when all the ROIs in the residual network were significant.

RESULTS

Activations

Haptically shape-selective regions (HS>HT) were located bilaterally in extensive regions spanning the postcentral sulcus (PCS) and the intraparietal sulcus (IPS), within which separable activations could be distinguished bilaterally in a number of regions: the PCS; anterior, posterior and ventral parts of the IPS (aIPS, pIPS and vIPS); the lateral occipital complex (LOC), ventral premotor cortex (PMv) and supplementary motor area (SMA). Unilateral activations could be resolved in the left postcentral gyrus, left precentral gyrus, left frontal eye field (FEF), left lingual gyrus, right middle frontal gyrus (MFG) and right anterior cingulate sulcus (aCS). Haptic texture-selectivity (HT>HS) was found bilaterally in a belt spanning the parietal operculum and posterior insula, with distinct activations in each of these regions, and in the right medial occipital cortex (MOC). Further details on these activations are in the report of Stilla and Sathian (2007). All 25 regions activated on these contrasts (20 from HS – HT and 5 from HT – HS) were used in the effective connectivity analysis.

In order to appreciate the import of the connectivity of these activated areas, which is the focus of the present report, it is necessary to consider the functions that are generally ascribed to them. These are briefly summarized here; for a fuller discussion see Stilla and Sathian (2007). The postcentral gyrus probably corresponds to Brodmann's area 1, and the PCS, to Brodmann's area 2, both sub-fields of primary somatosensory cortex (S1) (Geyer et al., 1999, 2000; Grefkes et al., 2001). The parietal opercular-posterior insular cortical belt extends over the three somatosensory fields OP1, OP4 and OP3 (posterolateral, anterolateral and anteromedial parietal operculum, respectively) defined by Eickhoff et al. (2006 a,b; 2007); these fields correspond to the second somatosensory cortex (S2), the parietal ventral area (PV) and the ventral somatosensory area (VS), respectively, of macaques. The aIPS, pIPS and vIPS are in or near multisensory regions (Grefkes et al., 2002; Saito et al., 2003; Stilla and Sathian, 2007). The LOC and MOC are both part of classical visual cortex, the LOC being an object-selective region (Malach et al., 1995) and the MOC probably corresponding to the second visual area, V2 (Stilla and Sathian, 2007). The precentral gyrus, FEF, PMv and SMA are usually considered motor areas while the MFG and aCS are implicated in cognitive functions. As pointed out in the Discussion, many of these areas have been found to be involved in roles

going beyond their originally discovered functions. Importantly for testing our hypotheses, the set of 25 ROIs includes regions in prefrontal (right MFG) and posterior parietal cortex (bilateral IPS) as well as in somatosensory cortex (PCS and parietal opercular-posterior insular cortex).

Effective connectivity

The Akaike information criterion (Akaike, 1974) yielded an optimum model order of one. The thresholded 25-ROI network obtained from the resulting MVAR is shown in Figure 1. It is evident that this is a very intricate network containing a great number of connections and is hence difficult to interpret. Therefore, it was subjected to network reduction, as described in Methods. 16 ROIs survived the reduction process; the significant connections in the reduced network are shown in Figure 2. It is to be noted that the contralateral homologs of most of the rejected ROIs were represented in the reduced network. This suggests that the reduction process tended to remove the redundancy arising from the inclusion of both left and right hemisphere regions (contralateral and ipsilateral to the stimulated hand, respectively) in the 25-ROI network. However, there were exceptions to this tendency. For example, both right and left vIPS ROIs were rejected, whereas both left and right pIPS were retained in the reduced network.

Table 1 lists the path weights for all connections in the reduced (16-ROI) network, with the significant paths identified in bold type. The arrows beside each path weight reflect the tendency of the BOLD signal in the two ROIs linked by the path to co-vary in the same direction, i.e. both tending to increase or decrease together ($\uparrow$), albeit with a phase difference; or vary in opposite directions, i.e. one tending to increase when the other tends to decrease ($\downarrow$); analogous to positive and negative correlations. Although these are henceforth referred to as “co-varying” and “anti-varying” paths for the sake of simplicity, it is important to recognize that this terminology does not imply excitatory vs. inhibitory connections at the neuronal level, since our inferences of Granger causality are based on hemodynamic responses, whose relationships with excitatory vs. inhibitory synaptic activity remain unclear (Stilla et al., 2007).

Study of the significant paths shown in Figure 2 and Table 1 indicates that interactions between ROIs even in the reduced network were highly complex. In many cases, interactions between pairs of ROIs were bidirectional and co-varying. Such interactions included those between visual and somatosensory areas: right LOC – left PCS, right LOC – right posterior insula; between a visual and a multisensory area: right LOC – left pIPS; between somatosensory areas: right parietal operculum – right posterior insula; between somatosensory and motor regions: left PCS – left FEF, left PMv – left postcentral gyrus, left pre- and postcentral gyri; between frontal and parietal foci: right MFG – left aIPS; and between left and right hemisphere homologs in the case of the SMA and the pIPS. In some instances, bidirectional interactions involving the left PCS (a somatosensory area) and other somatosensory (right parietal operculum, right posterior insula) or multisensory areas (left aIPS) were both anti-varying. Yet other interactions were unidirectional.

Consistent with its somatosensory processing function, the left PCS emerged as the strongest driver in the circuit, with 8 significant output paths compared to 5 significant input paths. Its connections were a mixture of co-varying and anti-varying paths. Its outputs were directed to parietal somatosensory and multisensory regions as well as occipital visual regions and the left FEF; its inputs were from a subset of these same regions. The left precentral gyrus was also a strong driver, with 5 outputs and only 1 input among significant paths. Its outputs, of which most were along co-varying paths, were directed to other motor cortical regions and to parietal sensory areas, both somatosensory and multisensory; its single significant input was from the (somatosensory) left postcentral gyrus, also a target of its output. The right posterior insula, another somatosensory region, was the source of 5 significant outputs, distributed among somatosensory, visual and motor areas, and the target of 3 significant inputs: from a

somatosensory, a multisensory and a visual area. Its significant connections tended to be mostly co-varying.

A motivating question for the present work is whether there are bottom-up somatosensory inputs into visual cortical areas, or whether cross-modal activation of visual cortex during somatosensory perception depends on top-down paths from prefrontal and posterior parietal cortex associated with visual imagery. Relevant to this issue, many significant connections of visual cortical areas (right LOC and right MOC) were with somatosensory cortex. The right LOC also had connections with other areas, including an input from the left PMv (a motor region) and reciprocal interactions with the left pIPS. There was no significant influence of any other frontal or parietal association region on visual cortical areas. Although the shape-selective right LOC was interconnected mostly with other shape-selective regions: left PMv, left PCS and left pIPS (reciprocally in the case of the latter two regions); it was also reciprocally connected with a texture-selective area, the right posterior insula. All significant paths involving the right LOC were co-varying. The texture-selective right MOC had only two significant inputs, a co-varying path from the texture-selective right posterior insula and an anti-varying path from the shape-selective left PCS.

DISCUSSION

Methodological considerations

The present study demonstrates that it is feasible to employ multivariate analysis of Granger causality to investigate effective connectivity in neural circuits using BOLD-fMRI data. The approach is more tractable than ESEM, and the multivariate implementation permits simultaneous analysis of interactions between multiple ROIs, thereby overcoming a key limitation of bivariate Granger causality analysis. Moreover, our procedures allow quantitative comparison of the weights of different paths in the network by omitting the conventional normalizing step, and also enable filtering out of influences mediated via intervening nodes included in the network, by computing partial coherence. The network reduction process is an advance that, together with significance thresholding using surrogate data, is helpful in focusing on the most critical interactions in the overall network.

It is worth emphasizing that there are limitations to this approach, which also apply to many other approaches to studying connectivity. One limitation specific to fMRI studies is that the inferred connectivity relies on measurements of the BOLD response, which is delayed and of necessity coarsely sampled relative to the neural events that trigger the hemodynamic responses. This raises a potential concern that inter-regional variability of the hemodynamic response function (HRF) (Aguirre et al., 1998; Silva et al., 2002; Handwerker et al., 2004) might give rise to spurious inferences of connectivity. However, simulations suggest that the impact of variable hemodynamic delays between regions, while increasing as sampling interval increases and path strength decreases, is in practice tolerable at sampling intervals up to 2 s (Deshpande, Sathian and Hu, 2008), which are quite realistic in fMRI studies. A second, more general limitation is that imposed by the methods used to select ROIs for connectivity analysis. A consequence of any set of selection criteria is that the entire network involved in the task may not enter the analysis. Thus, one must be careful not to assume that the “paths” that emerge are necessarily direct; they could be mediated through intermediate stations that may not be included in the network (although mediated influences within the network are removed by the partial coherence analysis). Moreover, an apparent directional influence between two ROIs could result from a common drive from a third region not within the network tested, if the paths from this region cause activity in one ROI to consistently lead that in the other. Hence, the circuits that emerge from Granger causality analysis should not be over-interpreted. In the present study, only cerebral cortical activations were considered, so that the role of subcortical structures in processing haptic shape and texture information remains open. Further, all ROIs

used for connectivity analysis were derived from the reciprocal contrasts between haptic shape and haptic texture conditions, implying that areas activated equally in both tasks (e.g., Brodmann's area 3b, Stilla and Sathian (2007)) did not enter the analysis. However, it is worth noting that selectivity for shape or texture in these regions was relative rather than absolute; i.e. most of these regions were active during discrimination of both shape and texture, but with a preference for one or other region (Stilla and Sathian, 2007). Moreover, the set of ROIs used for analysis of effective connectivity was appropriate for testing our hypotheses pertaining to the reasons for cross-modal recruitment of visual cortex during touch, since they included the visual cortical areas that were selectively active during haptic shape and texture perception, prefrontal-posterior parietal regions relevant to the top-down hypothesis, and somatosensory cortical regions relevant to the bottom-up hypothesis.

Effective connectivity during haptic perception

This study shows that, although effective connectivity in the network of haptically shape-selective and haptically texture-selective areas is rather complex, certain principles can be appreciated. Many of the significant paths in the present study linked regions to which varying functions have been attributed. For example, classical somatosensory cortical areas interacted not only with other somatosensory cortical areas but also with areas known to be multisensory, and those traditionally regarded as visual or motor. Similarly, so-called motor regions were interconnected with both motor and sensory regions, the latter including those traditionally thought to be somatosensory, visual, or multisensory. This underscores the complexity of the underlying circuits and suggests that the traditional separations between sensory and motor areas, or between somatosensory, visual and multisensory regions break down during natural behavior. Thus, while the LOC and MOC are both in visual cortex, the LOC has been repeatedly shown to be engaged during haptic shape perception (Amedi et al., 2001, 2002; James et al., 2002; Stilla and Sathian, 2007; Zhang et al., 2004) and the MOC, which probably corresponds to V2, was first identified by us as responsive during haptic texture perception (Stilla and Sathian, 2007). Conversely, the PCS, though a classical somatosensory area, is also shape-selective during visual perception (Stilla and Sathian, 2007). Together with corresponding findings in classical auditory cortex (Lakatos et al., 2007) these findings imply that multisensory processing is not restricted to the well-known regions along the IPS (Grefkes and Fink, 2005; Saito et al., 2003; Stilla and Sathian, 2007) but also characterizes a host of regions commonly thought to be unisensory.

Numerous studies have reported that tactile stimulation activates frontal regions involved in motor control, including primary motor cortex (Moore et al., 2000; Francis et al., 2000), the SMA (Bushara et al., 2001; Stilla and Sathian, 2007), PMv (Graziano et al., 1997; Stilla and Sathian, 2007) and the FEF (Stilla and Sathian, 2007). These activations in the "motor circuit" cannot be dismissed simply as reflecting preparation of motor output, since a motor response was either absent or controlled for in the cited studies. The analysis of effective connectivity in the present study corroborates the notion derived from these earlier studies, that a variety of regions and processes cooperate in behavior. The PMv is a particularly interesting area: while usually regarded as premotor in function, neurons in this region of macaques also show visual, somatosensory and multisensory responses (Graziano et al., 1997; Rizzolatti et al., 1998) and appear to be closely related to their parietal cortical counterparts (Rizzolatti et al., 1998). The sensory responses include those characterizing "mirror neurons", that fire not only during specific actions but also when the monkey sees another individual performing the same actions (Rizzolatti et al., 1998), and visual receptive fields that are anchored to the arm, shifting with the arm as it is moved (Graziano et al., 1997). This area is also implicated in the illusory incorporation of a synthetic hand into the body image with appropriate visual (Ehrsson et al., 2004) or somatosensory (Ehrsson et al., 2005) stimulation. The connectivity of the left PMv in the present study with both visual (right LOC) and somatosensory (left postcentral gyrus

and right posterior insula) regions is provocative in light of these earlier, intriguing observations, and these connections therefore merit further study.

With regard to the question of bottom-up somatosensory vs. top-down fronto-parietal inputs into visual cortical areas, the present study offers some evidence to support both possibilities. Both the visual cortical areas included in the reduced network, the right LOC and the right MOC, had a number of connections with somatosensory cortical areas. Both were driven by the left PCS (Brodmann's area 2) and the right posterior insula (OP3). This offers unequivocal evidence in favor of the second hypothesis, that there is bottom-up drive from somatosensory to visual cortex, presumably allowing somatosensory inputs to engage modality-independent representations that reside in what has classically been known as visual cortex. The right LOC also fed back to the left PCS. The only other visual cortical connections pertained to the right LOC, which was reciprocally connected with the left pIPS and also received an input from the left PMv. Apart from these, there were no direct paths from any part of fronto-parietal association cortex into visual cortical areas. While we cannot exclude a visual imagery role for the PMv input into the right LOC, the prefrontal cortical sector associated with content-specific top-down connectivity into visual cortex during visual imagery was more anterior (Mechelli et al., 2004). However, the left pIPS input into the right LOC could potentially reflect visual imagery, since its Talairach coordinates ($-10, -61, 55$) place it close to the superior parietal focus that Mechelli et al. (2004) found to be involved in content-independent connectivity with visual cortical areas during visual imagery. Thus, some evidence also emerges from the present study to support the first hypothesis, that visual imagery mediates cross-modal recruitment of visual cortex during haptic perception. Admittedly, support for this hypothesis would have been stronger had we found significant effective connectivity from prefrontal to visual cortex. It remains possible that such connectivity might occur under certain circumstances.

Overall, then, the present results are in agreement with those obtained in the more limited ESEM study with only five shape-selective ROIs (Peltier et al., 2007), i.e. supporting both bottom-up somatosensory drive of visual cortex and top-down parietal inputs possibly mediating visual imagery. In other words, both hypotheses are supported. This should not be interpreted as a lack of conclusiveness of the present study of effective connectivity. As pointed out earlier, there is no reason to assume that only one of the hypotheses should turn out to be correct. In fact, the existence of both bottom-up and top-down inputs into visual cortex is consistent with the notion that visual cortical areas contain modality-independent representations that are accessible not only through bottom-up sensory inputs, but also via top-down processes such as visual imagery (Sathian and Lacey, 2007). Definitive evidence for or against the visual imagery and multisensory integrative explanations for cross-modal recruitment of visual cortex will obviously require converging evidence from other lines of work.

The reciprocal connection between the right LOC and left pIPS is particularly interesting. We reported earlier that, among a set of five paired areas that were shape-selective in both vision and touch (PCS, aIPS, pIPS, vIPS and LOC), only the right LOC and left pIPS showed significant correlations across subjects between the magnitudes of activity during haptic and visual shape discrimination (Stilla and Sathian, 2007). Based on this finding, we proposed a special role for these two regions in multisensory integration of shape (Stilla and Sathian, 2007). The present study adds to the evidence linking the functional role of these two regions in shape perception based on their significant reciprocal connectivity. To what extent this connectivity reflects visual imagery remains uncertain (see above). As noted by Stilla and Sathian (2007), selectivity for haptic shape vs. texture, as assessed by direct contrasts between these two conditions, appears to be, in general, quantitative rather than qualitative, since most regions were responsive in both conditions but with different magnitudes of BOLD response. The correlates of such selectivity at the neuronal level remain unknown. The effective

connectivity analysis of the present study reinforces the idea of relative rather than absolute selectivity, since regions selective for shape or texture were not linked exclusively with regions exhibiting the same preference.

CONCLUSIONS

We conclude that it is feasible to employ multivariate Granger causality analysis followed by network reduction to eliminate regions whose connectivity does not contribute significantly, to assess effective connectivity within a network of active regions, thereby fulfilling the secondary aim of the present study. Effective connectivity within the circuit of haptic shape-selective and haptic texture-selective regions is quite complex, involving interactions between areas usually regarded as somatosensory, multisensory, visual and motor. This points to flexible cooperation between these different functional regions, rather than stereotyped separations of function. With respect to the primary aim of the present study, clear support was found for the existence of bottom-up, somatosensory inputs into visual cortical areas (hypothesis 1), and some support was also found for a role for top-down inputs potentially mediating visual imagery, from postero-supero-medial parietal cortex (hypothesis 2). The findings fit with the idea of modality-independent representations that can be accessed by both bottom-up sensory inputs and top-down processes such as visual imagery.

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Figure 1.
The 25-ROI network including only the significant connections ($p < 0.05$).

Figure 2.
The reduced 16-ROI network including only the significant connections ($p < 0.05$).

Table 1

Path weights of the reduced 16-ROI network shown in Fig. 2. The significant paths are shown in bold face. ↑ denotes co-varying and ↓ denotes anti-varying paths.

	L SMA	R SMA	L PM V	L FEF	L preC G	L postC G	LL G	R MF G	L PCS	L aIPS	L pIP S	R pIP S	R LOC	R MOC	R par oper	R post ins
	47↑	47↑	2↑	2↑	14↑	6↓	0↓	7↑	2↑	2↑	1↓	1↓	0↓	0↑	2↑	3↑
	-	-	0↑	0↑	9↑	1↓	4↓	3↓	5↑	0↑	2↓	1↓	0↓	1↑	1↑	0↑
	9↑	0↑	-	26↑	24↓	17↑	3↓	0↓	1↑	3↑	1↓	0↓	7↑	2↑	1↑	11↑
	1↓	0↑	9↑	-	11↑	0	0↓	0↓	16↑	1↑	3↑	0↓	0↑	0↑	2↑	1↑
	6↑	2↑	7↑	9↑	-	62↑	0↓	1↓	0↑	10↑	0↑	0↓	0↑	2↑	1↑	0↑
	6↑	0↑	18↑	1↑	128↑	-	0↓	1↓	1↑	0↑	1↓	0↓	0↑	1↑	4↓	3↑
	0↑	2↓	1↑	1↑	0↓	0↓	-	0↓	0↑	1↑	1↑	14↓	1↓	4↑	0↓	2↑
	20↑	6↑	0↑	0↑	4↓	2↑	0↓	-	1↓	38↑	0↑	4↓	1↑	0↑	0↓	10↑
	1↓	4↑	1↑	36↑	0↑	1↓	0↓	0↓	-	14↓	2↓	5↑	12↑	9↑	18↓	12↓
	1↓	0↑	1↑	1↑	11↑	0↓	0↓	13↑	14↓	-	2↓	0↓	0↑	1↑	0↓	21↑
	7↓	7↓	2↑	25↑	7↑	8↓	2↓	0↑	15↓	17↑	-	23↑	8↑	0↑	0↓	0↑
	1↓	1↑	0↑	0↑	1↑	1↓	9↑	4↑	13↑	0↑	10↑	-	1↑	2↑	0↓	4↑
	2↓	1↓	16↑	3↑	2↑	4↓	4↓	2↑	17↑	0↑	16↑	2↓	-	0↑	0↓	17↑
	0↑	1↓	0↑	0↑	3↑	1↓	2↓	0↑	12↓	1↑	0↓	1↓	0↓	-	3↑	11↑
	4↑	1↓	0↑	2↑	3↑	8↓	0↑	0↑	47↓	1↑	0↑	0↓	0↓	5↑	-	131↑
	2↑	0↓	3↑	0↑	0↑	2↓	1↓	3↑	14↓	19↑	0↑	2↓	10↑	8↑	56↑	-