Where Bottom-up Meets Top-down: Neuronal Interactions during Perception and Imagery

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Functional magnetic resonance imaging (fMRI) studies have identified category-selective regions in ventral occipito-temporal cortex that respond preferentially to faces and other objects. The extent to which these patterns of activation are modulated by bottom-up or top-down mechanisms is currently unknown. We combined fMRI and dynamic causal modelling to investigate neuronal interactions between occipito-temporal, parietal and frontal regions, during visual perception and visual imagery of faces, houses and chairs. Our results indicate that, during visual perception, category-selective patterns of activation in extrastriate cortex are mediated by content-sensitive forward connections from early visual areas. In contrast, during visual imagery, category-selective activation is mediated by content-sensitive backward connections from prefrontal cortex. Additionally, we report content-unrelated connectivity between parietal cortex and the category-selective regions, during both perception and imagery. Thus, our investigation revealed that neuronal interactions between occipito-temporal, parietal and frontal regions are task- and stimulus-dependent. Sensory representations of faces and objects are mediated by bottom-up mechanisms arising in early visual areas and top-down mechanisms arising in prefrontal cortex, during perception and imagery respectively. Additionally non-selective, top-down processes, originating in superior parietal areas, contribute to the generation of mental images, regardless of their content, and their maintenance in the 'mind's eye'.

Keywords: dynamic causal modelling, functional magnetic resonance imaging, visual imagery, visual perception

Introduction

Functional brain imaging studies have shown that within the human ventral vision pathway, faces and other objects, such as outdoor scenes, houses, chairs, animals, tools and human body parts, have distinct patterns of activations (Martin *et al.*, 1996; Kanwisher *et al.*, 1997; Aguirre *et al.*, 1998; Cappa *et al.*, 1998; Epstein and Kanwisher, 1998; Chao *et al.*, 1999; Haxby *et al.*, 1999; Ishai *et al.*, 1999; Puce *et al.*, 1999; Thompson-Schill *et al.*, 1999; Downing *et al.*, 2001; Devlin *et al.*, 2002). In particular, it has been shown that houses, faces and chairs evoke maximal responses in distinct ventral occipito-temporal regions and that these regions have a topological arrangement that is consistent across subjects (Ishai *et al.*, 1999, 2000a). Rather than activating discrete, segregated areas, each category was associated with its own differential pattern of responses across a broad expanse of cortex. It has therefore been proposed that the representation of objects in the ventral stream is not restricted to small, highly selective patches of cortex, but is a distributed representation of information about object form (Ishai *et al.*, 1999, 2000a; Haxby *et al.*, 2001).

Although it is unclear to what extent category-selective responses are mediated by bottom-up and top-down mechanisms, empirical evidence indicates that both processes may modulate these content-specific patterns of activation. A recent study, investigating the neuronal interactions that mediate activity during passive viewing and delayed matching tasks of faces and objects, has shown that category effects in occipito-temporal cortex were mediated by forward connections from early visual areas (Mechelli *et al.*, 2003). Specifically, the connectivity from inferior occipital cortex to the 'house-responsive' regions was stronger during the perception of houses than any other category. Similarly, the connectivity from inferior occipital cortex to the 'face-responsive' regions was stronger during the perception of faces. Finally, the connectivity from inferior occipital cortex to the 'chair-responsive' regions was stronger during the perception of chairs. These findings indicate that category-selective patterns of activation in the ventral pathway are engendered by the visual input. As pictures of houses, faces and chairs contain different visual attributes, the functional specialization observed in occipito-temporal cortex is likely to be the result of a hierarchical, bottom-up, 'feature' analysis. The category-specific enabling of forward connections demonstrated in Mechelli *et al.* (2003) is consistent with the functional segregation of visual information as it is conveyed to higher cortical levels.

In contrast, empirical evidence indicates that neural activation within the category-responsive regions is modulated by expertise (Gauthier *et al.*, 2000), selective attention (O'Craven *et al.*, 1999), mental imagery (Ishai *et al.*, 2000b, 2002; O'Craven and Kanwisher, 2000) and emotion (Vuilleumier *et al.*, 2001). Of special interest are studies showing category-related activation in the absence of pictorial stimuli. For example, reading the names of animals and tools evoked category-related responses in the same regions activated by pictures of animals and tools (Chao *et al.*, 1999). Moreover, visual imagery studies have shown that in the absence of retinal input, the generation of mental images of faces and other objects evoked content-related activation in the corresponding visual areas (Ishai *et al.*, 2000b, 2002; O'Craven and Kanwisher, 2000; Kosslyn and Thompson, 2003). Taken collectively, these studies strongly indicate top-down mechanisms, which are likely originated in prefrontal and parietal areas.

The aim of the present study was to investigate the neuronal interactions that mediate content-related activation in the occipito-temporal cortex of the human brain, using functional magnetic resonance imaging (fMRI) and dynamic causal modelling (DCM; Friston *et al.*, 2003). To that end, we compared the effective connectivity between occipito-temporal, parietal and frontal regions, while subjects performed two cognitive tasks, namely passive viewing and visual imagery of faces, houses and

chairs. We hypothesized that the category-specific patterns of activation observed in occipito-temporal cortex during perception could be explained by a selective enabling forward connectivity from early visual areas. In contrast, we predicted that content-related activation observed in occipito-temporal cortex during visual imagery would be associated with category-dependent changes in backward connectivity from parietal and frontal areas. Furthermore, we examined whether parietal and frontal regions exhibit different patterns of effective connectivity during visual imagery of faces, houses and chairs, as previous fMRI studies have not shown category-specific imagery activation within these regions (Ishai *et al.*, 2000b).

We report that during visual perception, when subjects viewed gray-scale pictures of faces, houses and chairs, the category selective effects in occipito-temporal cortex were mediated by forward connections from early visual areas. In contrast, during visual imagery, when subjects generated mental images of faces, houses and chairs from long-term memory, the category selective effects in occipito-temporal cortex were mediated by backward connections from prefrontal cortex. While the backward connections from prefrontal cortex to occipito-temporal cortex were category-selective, the backward connections from superior parietal cortex were not content-specific. Thus, our analysis revealed that dynamic neuronal interactions between occipito-temporal, parietal and frontal regions are task- and stimulus-dependent. Sensory representations of faces and objects in ventral extrastriate cortex, are mediated by bottom-up mechanisms arising in early visual areas and top-down mechanisms originating in prefrontal cortex, during perception and imagery respectively. Additionally, non-selective, top-down processes, originating in superior parietal areas, contribute to the generation of mental images and their maintenance in the 'mind's eye.'

Materials and Methods

Subjects

Five normal, right-handed subjects (two males, three females, age 28 ± 5 years), with normal vision, participated in this study. These subjects were originally reported in Ishai *et al.* (2000b) and were selected, for the purpose of our investigation, because the data were acquired with whole brain coverage. All subjects gave written informed consent for the procedure in accordance with protocols approved by the NIMH institutional review board.

Experimental Design

A block design was used, with four experimental conditions: visual perception, perception-control, visual imagery and imagery-control. In the visual perception condition, gray scale photographs of houses, faces and chairs were presented at a rate of 1/s for 21 s. Subjects were instructed to view the stimuli. In the perception-control condition, scrambled pictures were presented at a rate of 1/s for 21 s with identical instructions. In the imagery condition, a gray square was presented for 21 s. Subjects were instructed to generate vivid images of familiar houses, faces and chairs from long-term memory, while looking at the gray square and press a button when ready with a vivid image. On average, subjects generated seven images with a mean duration of 2.5 s and there was no significant difference between faces, houses, or chairs in terms of number of images generated and their duration. In the imagery-control condition, a gray square was presented for 21 s and subjects were instructed to view the gray square. None of the subjects reported spontaneous imagery during the imagery-control condition. Before the scanning session, subjects were pre-trained with the perception and imagery tasks. The percep-

tion and imagery tasks were acquired as alternating, separate time series. During the perception task, the perception condition alternated with the perception-control condition. Similarly, during the imagery task, the imagery condition alternated with the imagery-control condition. During perception and imagery tasks, the order of category blocks was counterbalanced across subjects.

Data Acquisition

A 1.5 T General Electric Signa scanner was used to acquire blood oxygen level-dependent (BOLD) T_2^*-weighted MRI images using a gradient-echo echoplanar sequence (T_R = 3 s, T_E = 40 ms, FOV = 20 cm, 64 × 64 matrix, voxel size = 3.125 × 3.125 × 5 mm). Each functional image comprised 24 contiguous, 5 mm thick axial slices to cover the whole brain. The same scanner was used to acquired high-resolution full volume structural images (T_R = 13.9 s, T_E = 5.3, FOV = 20 cm, 256 × 256 matrix). Each structural image comprised 124, 1.5 mm thick sagittal slices.

Statistical Parametric Mapping

The aim of the present study was to test the hypothesis that content-related activation in the occipito-temporal cortex is mediated by increased connectivity from early visual areas and fronto-parietal areas, during perception and imagery respectively. Thus, we performed a conventional statistical parametric mapping analysis to identify task- and content-related activation within our regions of interest. Statistical parametric mapping analysis (Friston *et al.*, 1995) was performed using SPM2 software (Wellcome Department of Imaging Neuroscience, London, UK. http//www.fil.ion.ucl.ac.uk/spm), running under Matlab 6 (Mathworks Inc., Sherbon MA). Functional images were realigned, normalized and smoothed using a Gaussian filter of 6 mm. A series of subject-specific models were created to characterize the hemodynamic response under each experimental condition. The data were high-pass filtered using a set of discrete cosine basis functions with a cutoff period of 512 s. The analysis used the general linear model to identify significant task- and content-related activation in our regions of interest. These included the occipito-temporal, superior parietal and prefrontal cortices for perception and imagery; and the occipito-temporal cortex for the category effects common to perception and imagery. Inferences were made at *P* < 0.001 (uncorrected for multiple comparisons), with an extent threshold for each cluster of five voxels. A detailed report and discussion of the functional data from our five subjects, across the whole brain, can be found in Ishai *et al.* (2000b). Although hemispheric asymmetry has been reported, with stronger activity in the right hemisphere during perception and stronger activity in the left hemisphere during imagery (Ishai *et al.*, 2000b), category-related responses were found in both hemispheres during both tasks. In the current study we focused our analysis on the left hemisphere for computational expediency.

Dynamic Causal Modelling

Finally, we used DCM (Friston *et al.*, 2003) as implemented in SPM2. The aim of DCM is to estimate and make inferences about the influence that one neural system exerts over another and how this is affected by the experimental context. In DCM, three distinct sets of connectivity parameters are estimated. A first set of parameters scale the direct and extrinsic influence of inputs on brain states in any particular region. These parameters are generally of little interest in the context of DCM but, of course, are the primary focus in classical analyses of regionally specific effects. A second set of parameters refer to the 'intrinsic connections' that couple neuronal states in different regions. These parameters allow one to estimate the impact that one neural system exerts over another, in the absence of experimental perturbations. A third set of parameters, or 'bilinear terms', reflects changes in the intrinsic coupling between regions that are induced by experimental manipulation. These parameters allow one to estimate the impact that an experimental manipulation exerts on a pathway as opposed to a cortical region and are the primary focus of the present investigation.

DCM uses a previously validated biophysical model of fMRI measurements (Friston *et al.*, 2000; Mechelli *et al.*, 2001) to estimate the underling neuronal activity from the observed hemodynamic

response. The estimated underlying neuronal activity is then used to derive the connectivity parameters (for details, see Friston *et al.*, 2003; Mechelli *et al.*, 2003). In brief, these two steps are repeated iteratively and correspond to the expectation and maximization steps of an EM algorithm. The intrinsic connections estimate the rate of change of neuronal activity in one area induced by activity in another. As such, this characterization does not depend on the units of activity *per se*, but the 'speed' or rate of inter-regional influences.

Since the perception and imagery tasks were acquired as separate time series, they were treated as such in our DCM analysis. A series of subject-specific dynamic causal models were constructed, which included those regions showing significant effects in the statistical parametric mapping analysis. Specifically, a visual perception network was constructed which included the inferior occipital cortex, prefrontal cortex, superior parietal cortex and the category-responsive regions in the occipital and temporal cortex. As depicted in Figure 1 (left), the network comprised of forward and backward connections between the category-responsive areas and the remaining regions in the network and between the prefrontal cortex and the superior parietal cortex. Additional connectivity parameters (i.e. bilinear terms) were specified to look at the influence of object category on all backward and forward connections between the category-responsive areas and the remaining regions in the network. The stimulus function, that encoded the visual presentation of houses, faces and chairs, entered the dynamic causal model through the sensory area, i.e. inferior occipital cortex. The resulting perturbation was then allowed to propagate throughout the model via interconnections between inferior occipital cortex and the remaining regions. In addition, a visual imagery network was constructed which included the precuneus, prefrontal cortex, superior parietal cortex and the category-responsive regions in the occipital and temporal cortex. As

shown in Figure 1 (right), the network comprised of forward and backward connections between the category-responsive areas and the remaining regions in the network and between the prefrontal cortex and the superior parietal cortex. Additional connectivity parameters (i.e. bilinear terms) were specified to look at the influence of object category on all backward and forward connections between the category-responsive areas and the remaining regions in the network. The stimulus function, that encoded the visual imagery of houses, faces and chairs, entered the dynamic causal model through prefrontal and superior parietal cortices. The resulting perturbation was then allowed to propagate throughout the model via interconnections between prefrontal cortex, superior parietal cortex and the remaining regions. Critically, the visual perception and visual imagery networks included the same category-responsive regions in occipital and temporal cortex.

Subject-specific regions (8 mm-radius) were selected on the basis of the regional activations detected with statistical parametric mapping. When more than one activation peak was found within the same region of interest, the maxima of the SPM{T} within that region was selected. Regional activities were defined in terms of principal eigenvariates and were extracted in a subject-specific fashion. The resulting values were entered into the DCM to estimate the forward and backward 'intrinsic connections' (i.e. the impact that a region exerts over another in the absence of experimental perturbation) and the 'bilinear terms' (i.e. the impact of object category on the intrinsic connections), for each subject independently. Statistical inferences are based upon the probability that the connectivity parameters exceeded 0 with 95% confidence. It should be noted that correction for multiple comparisons is not required in DCM as there are no null hypotheses tested in a classical sense. Rather, the probability that an estimated
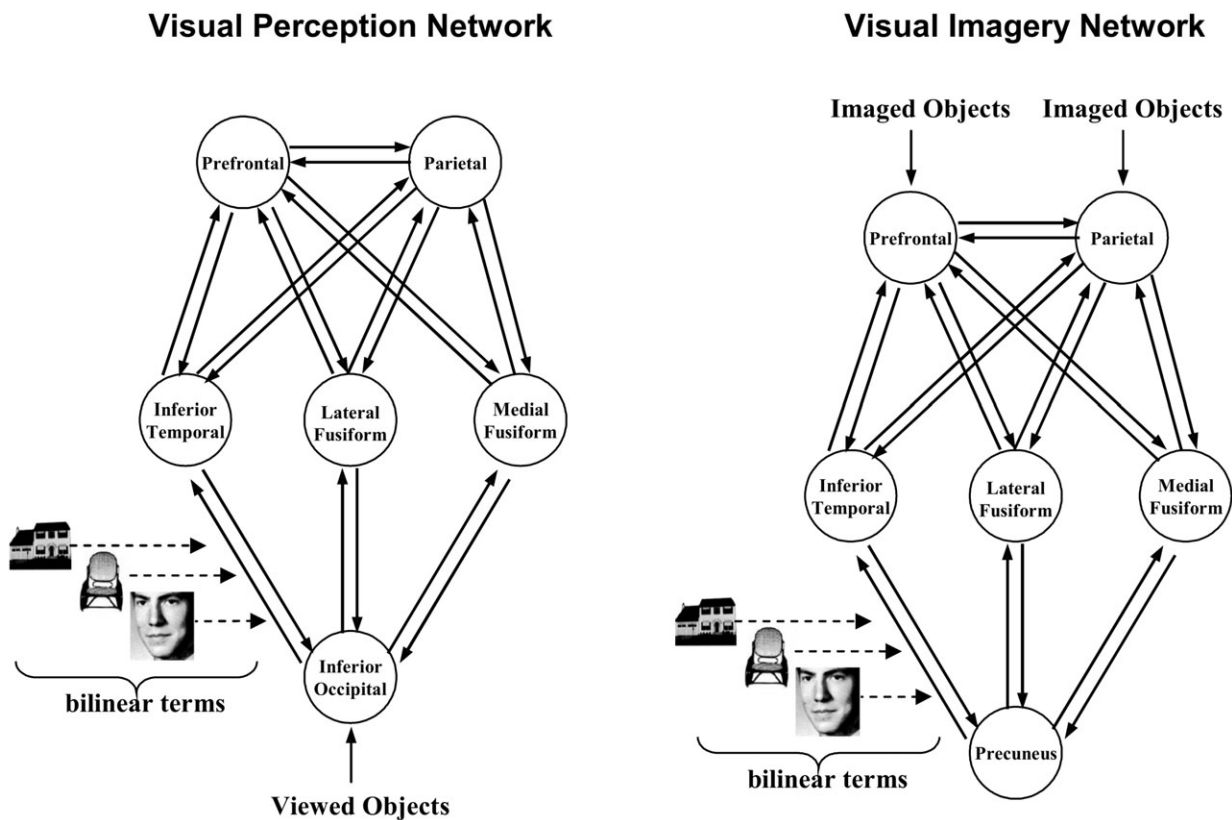
Figure 1. The visual perception (left) and visual imagery (right) networks used for the DCM analysis. The visual perception network comprised of both category-responsive regions in the occipito-temporal cortex and non-selective regions (inferior occipital cortex, prefrontal cortex and superior parietal cortex). The vector 'Visual Objects' encoded the visual presentation of houses, faces and chairs and entered the visual perception network through the 'input area' in inferior occipital cortex. The visual imagery network also comprised of both category-responsive regions in the occipito-temporal cortex and non-selective regions (precuneus, prefrontal cortex, superior parietal cortex). The vector 'Imaged Objects' encoded the visual imagery of houses, faces and chairs and entered the visual imagery network through prefrontal and superior parietal cortices. DCM was used to estimate bilinear terms for all forward and backward connections, in the visual perception and the visual imagery models independently.

connectivity parameter lies in a certain range of values (e.g. $0 \rightarrow \infty$) is computed within a Bayesian framework (Friston *et al.*, 2003).

Results

Statistical Parametric Mapping

The statistical parametric mapping analysis identified two cortical networks that were activated during visual perception and visual imagery, respectively (see Table 1 and Fig. 2). The inferior occipital cortex, superior parietal cortex and a number of regions in the occipital and temporal cortex showed greater activation during visual perception relative to perception-control ($P < 0.001$, uncorrected); see Figure 2a. The inferior occipital and superior parietal cortex did not exhibit category-selective activation, even with a lower statistical threshold ($P < 0.05$, uncorrected). In contrast, the remaining regions in occipito-temporal cortex showed significant category effects ($P < 0.001$, uncorrected); see Figure 2c. Specifically, a region in the medial portion of the fusiform gyrus responded more to houses than chairs and faces (4/5 subjects); an adjacent region in the lateral fusiform gyrus and occipito-temporal sulcus responded more to faces than houses and chairs (5/5 subjects); and a more lateral region in the inferior temporal gyrus responded more to chairs than houses and faces (5/5 subjects).

The precuneus, superior parietal cortex, prefrontal cortex and a number of regions in occipito-temporal cortex showed greater activation during visual imagery relative to imagery-control ($P < 0.001$, uncorrected); see Figure 2b. The precuneus, superior parietal and prefrontal cortex did not exhibit category-selective activation, even with a lower statistical threshold ($P < 0.05$, uncorrected). In contrast, the remaining regions in the occipito-temporal cortex showed significant category effects ($P < 0.001$, uncorrected); see Figure 2c. Specifically, a region in the medial portion of the fusiform gyrus responded more during imagery of houses than imagery of chairs and faces (4/5 subjects); an adjacent region in the lateral fusiform gyrus and occipito-temporal sulcus responded more during imagery of faces than imagery of houses and chairs (5/5 subjects); and a more lateral region in the inferior temporal gyrus responded more during imagery of chairs than imagery of houses and faces (5/5 subjects). See Ishai *et al.* (2000b) for a detailed report and discussion of the functional data from our five subjects outside our regions of interest.
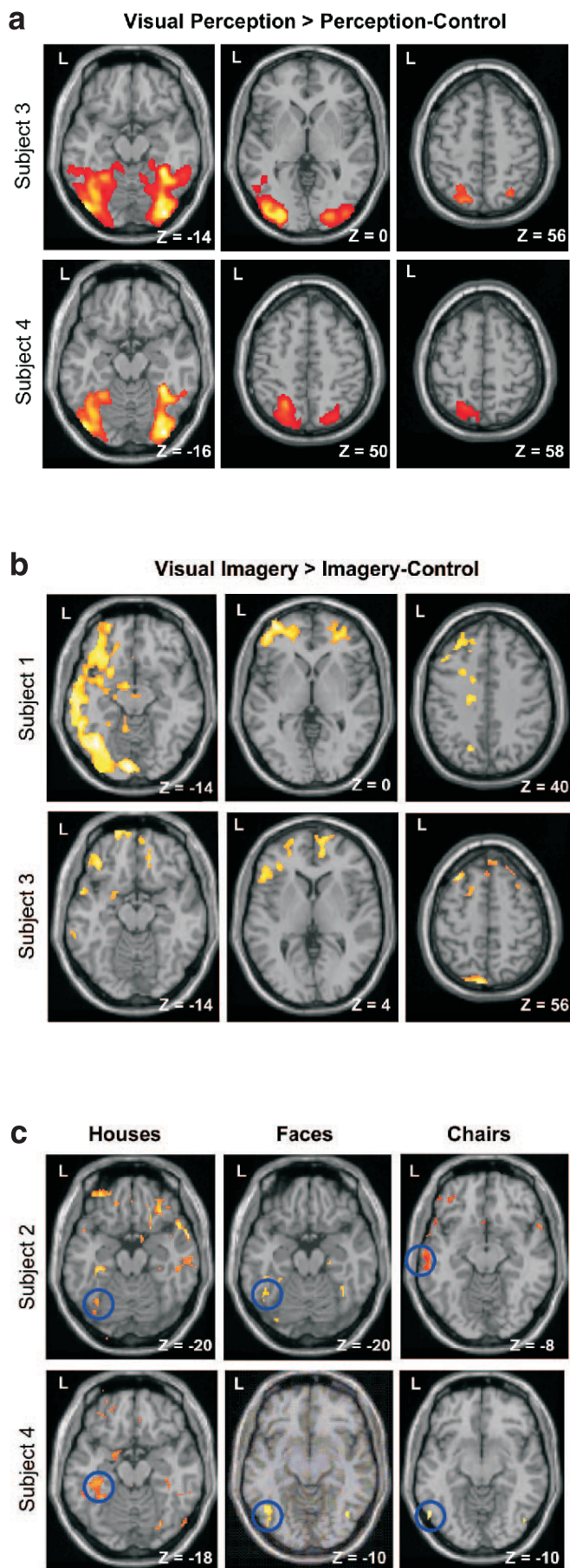
Dynamic Causal Modelling

The regions identified by the statistical parametric mapping analysis were used to construct a series of subject-specific dynamic causal models. A visual perception network was constructed, which included inferior occipital cortex, superior parietal, prefrontal cortex and the category-responsive regions in the occipito-temporal cortex (see Fig. 1, left). In addition, a visual imagery network was constructed, which included the precuneus, superior parietal, prefrontal cortex and the category-responsive regions in the occipito-temporal cortex (see Fig. 1, right). Critically, the two networks included the same category-responsive regions that showed content-related activity during both visual perception and visual imagery. The visual perception and visual imagery networks comprised forward and backward connections between regions, as represented graphically in Figure 1. Additional connectivity parameters (i.e. bilinear terms) were also specified to investigate the influence of object category on the backward and forward

Table 1

Significant activations within our regions of interest, identified in a subject-specific fashion using statistical parametric mapping

	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5
Perception > perception-control					
Inferior occipital	−22 −86 −10 (4.7)	−28 −84 −8 (8.3)	−34 −86 −10 (6.2)	−34 −72 −12 (8.3)	−26 −94 0 (8.9)
Superior parietal	−28 −58 64 (6.7)	−40 −62 50 (4.8)	−32 −52 56 (3.8)	−20 −72 54 (7.3)	−22 −60 52 (8.5)
Mid-occipital	−38 −82 −16 (6.6)	−44 −74 −12 (6.2)	−42 −80 −14 (4.2)	−44 −80 −16 (7.6)	−46 −76 −12 (7.5)
Imagery > imagery-control					
Precuneus	−10 −52 24 (3.2)	−20 −98 10 (4.1)	−8 −62 26 (3.3)	−8 −94 18 (5.2)	−20 −54 34 (5.6)
Superior parietal	−16 −66 40 (5.0)	−16 −78 60 (6.0)	−6 −80 56 (7.5)	−16 −80 54 (7.2)	−10 −64 48 (5.0)
Mid-frontal	−36 58 0 (6.8)	−24 60 28 (5.0)	−4 50 12 (3.3)	−34 46 −4 (5.3)	−26 46 12 (5.3)
Category-effects (common to perception and imagery)					
Chairs > faces and houses					
Inferior temporal		−66 −36 −8 (3.5)		−52 −66 −8 (3.6)	−46 −72 −10 (4.3)
Mid-temporal	−46 −82 10 (5.8)		−46 −72 −10 (3.1)		
Faces > houses and chairs					
Mid-fusiform				−32 −56 −14 (3.8)	−30 −40 −12 (3.2)
Posterior fusiform	−38 −74 −24 (5.7)	−38 −76 −20 (4.1)	−24 −84 4 (3.4)		−22 −74 −12 (4.1)
Houses > chairs and faces					
Medial fusiform	−34 −72 −14 (5.0)	−34 −66 −20 (3.1)		−36 −66 −18 (3.1)	−24 −62 −6 (3.2)

Visual perception > perception-control: regions that showed greater activation during visual perception relative to perception-control ($P < 0.001$ uncorrected). These regions did not show any category effects, even with a lower statistical threshold ($P < 0.05$, uncorrected). Visual imagery > imagery-control: regions that showed greater activation during visual imagery relative to imagery-control ($P < 0.001$ uncorrected). These regions did not show any category effects, even with a lower statistical threshold ($P < 0.05$, uncorrected). Category effects (common to perception and imagery): regions that showed greater activation during visual perception relative to perception-control; during visual imagery relative to imagery-control; and for one object category relative to the other two.

a Visual Perception > Perception-Control

Subject 3 / Subject 4

b Visual Imagery > Imagery-Control

Subject 1 / Subject 3

c Houses / Faces / Chairs

Subject 2 / Subject 4

connections. DCM was then used to estimate the connectivity parameters of the two networks, independently for each subject (see Materials and Methods for details).

Intrinsic Connections

Intrinsic connections refer to the impact that one region exerts over another in the absence of experimental perturbation and can be regarded as 'baseline' connectivity established by the experimental context (i.e. task-set). During perception, a number of forward and backward connections between inferior occipital cortex, superior parietal and the category-responsive regions were significantly greater than 0 in most subjects. In contrast, the forward and backward connections between prefrontal cortex and the category-responsive regions were not significant in any of the subjects (see Tables 2 and 3). Similarly, during imagery, a number of intrinsic connections between the precuneus, superior parietal and the category-responsive regions were significantly greater than 0 in most subjects. In contrast, the forward and backward connections between prefrontal cortex and the category-responsive regions were not significant in any subject (see Tables 4 and 5). These findings indicate that during perception, the category-responsive regions were functionally connected with inferior occipital cortex and superior parietal cortex, while during imagery, the category-responsive regions were functionally connected with precuneus and superior parietal cortex.

Influence of Object Category on the Intrinsic Connections

The influence of object category on the intrinsic connections was the primary focus of our DCM investigation. We found that, during visual perception, content-related activation in occipito-temporal cortex was mediated by increased connectivity from inferior occipital cortex in all five subjects. Thus, the intrinsic connectivity from inferior occipital cortex to the 'house-responsive' region was stronger during the presentation of houses than any other category; the intrinsic connectivity from inferior occipital cortex to the 'face-responsive' region was strongest during the presentation of faces; and the intrinsic connectivity from inferior occipital cortex to the 'chair-responsive' region was strongest during the presentation of chairs. In contrast, content-related activation in the occipito-temporal cortex was not mediated by increased connectivity from prefrontal cortex or superior parietal cortex. Thus, the intrinsic connectivity between prefrontal cortex, superior parietal and the category responsive regions was similar during the presentation of house-, face- and chair-stimuli (see Tables 2 and 3). These results are consistent with our prediction that content-related activation during visual perception is mediated by bottom-up mechanisms, arising in early visual areas.

During visual imagery, content-related activation in occipito-temporal cortex was mediated by increased connectivity from

Figure 2. Activations as identified using statistical parametric mapping at $P < 0.001$. (*a*) Regions showing increased activity during visual perception relative to perception-control in subjects 3 and 4. (*b*) Regions showing increased activity during visual imagery relative to imagery-control in subjects 1 and 3. (*c*) Regions showing greater activation for one object-category relative to the others (i.e. houses > faces and chairs; faces > houses and chairs; and chair > houses and faces), during both visual perception and visual imagery in subjects 2 and 4. The blue circle indicates the category-sensitive regions in the occipito-temporal cortex which were selected for the DCM analysis. A number of regions outside the occipito-temporal cortex also showed category-sensitive activation, but there were no replications across subjects.

Table 2

Subject-specific connectivity parameters during visual perception, as identified by dynamic causal modelling

Visual perception	Subject 1				Subject 2				Subject 3				Subject 4				Subject 5			
	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C
Forward connections																				
Inf. occipital → house-responsive	**0.34**	**0.34**	−0.17	−0.26	**0.31**	**0.41**	−0.13	−0.16	–	–	–	–	**0.40**	**0.43**	−0.34	0.13	0.11	**0.29**	−0.11	−0.05
Inf. occipital → chair-responsive	**0.29**	0.10	**0.24**	−0.30	**0.25**	−0.25	**0.15**	−0.15	0.19	−0.39	**0.37**	0.16	**0.71**	−0.13	**0.34**	0.14	**0.76**	−0.10	**0.59**	−0.09
Inf. occipital → face-responsive	**0.66**	−0.26	−0.15	**0.23**	−0.18	−0.28	−0.27	**0.40**	0.07	−0.07	−0.22	**0.19**	**0.44**	0.11	−0.20	**0.31**	**0.25**	0.12	−0.19	**0.28**
House-responsive → sup. parietal	0.11	0.10	0.10	−0.01	**0.57**	−0.20	0.01	0.00	–	–	–	–	**0.61**	0.03	0.01	0.13	**0.23**	0.06	0.08	−0.06
Chair-responsive → sup. parietal	**0.72**	0.06	0.07	0.05	−0.36	−0.20	0.00	0.01	−0.02	−0.37	0.16	0.20	**0.48**	0.07	−0.31	0.12	**0.44**	0.13	−0.04	0.27
Face-responsive → sup. parietal	**0.40**	0.07	−0.04	0.19	−0.74	−0.27	0.00	0.00	**0.30**	0.05	−0.06	0.11	**0.69**	0.31	−0.06	0.06	**0.76**	0.10	0.07	0.17
House-responsive → mid-frontal	0.07	0.01	0.00	0.00	−0.11	0.01	−0.01	0.06	–	–	–	–	0.03	0.00	0.01	−0.02	−0.01	0.00	0.00	−0.04
Chair-responsive → mid-frontal	0.14	0.01	−0.01	0.01	−0.00	0.00	0.00	−0.03	−0.07	0.01	0.00	0.01	0.01	0.01	0.00	0.00	0.12	0.01	0.01	0.00
Face-responsive → mid-frontal	0.12	−0.02	−0.06	0.05	−0.05	0.00	0.01	0.00	0.01	0.00	−0.02	−0.02	−0.05	0.06	−0.11	0.01	0.04	0.00	0.01	0.00
Sup. parietal → mid-frontal	0.03	–	–	–	0.02	–	–	–	0.04	–	–	–	0.00	–	–	–	0.01	–	–	–
Backward connections																				
House-responsive → inf. occipital	**0.21**	0.00	0.00	−0.02	**0.44**	−0.17	−0.03	−0.02	–	–	–	–	**0.22**	0.06	−0.04	0.20	**0.55**	0.02	0.16	−0.11
Chair-responsive → inf. occipital	**0.33**	−0.02	0.02	0.00	−0.08	−0.08	0.03	−0.06	**0.23**	−0.01	0.00	0.00	0.14	−0.06	0.08	0.06	**0.21**	−0.01	0.05	−0.07
Face-responsive → inf. occipital	**0.20**	0.01	0.02	0.02	**0.57**	−0.13	−0.08	−0.01	**0.27**	0.00	0.00	0.01	0.03	0.03	−0.03	0.08	**0.19**	0.06	0.00	−0.01
Sup. parietal → house-responsive	0.12	−0.04	0.00	0.00	**0.20**	0.00	0.00	0.00	–	–	–	–	**0.25**	0.03	0.00	0.03	0.04	−0.03	0.01	0.01
Sup. parietal → chair-responsive	**0.38**	−0.07	−0.05	0.01	−0.12	0.01	0.00	0.00	−0.02	−0.01	0.00	0.00	**0.28**	0.02	0.02	0.12	**0.34**	0.12	0.12	−0.05
Sup. parietal → face-responsive	**0.23**	−0.12	0.11	0.05	0.02	−0.02	0.02	0.00	0.01	0.00	−0.01	0.02	0.03	0.03	0.01	0.14	0.00	0.03	0.00	−0.04
Mid-frontal → house-responsive	−0.09	0.00	0.00	0.04	0.00	0.00	0.01	0.00	–	–	–	–	−0.41	0.12	−0.06	0.01	−0.02	0.01	0.00	0.00
Mid-frontal → chair-responsive	−0.03	0.01	0.00	−0.03	−0.11	−0.04	0.03	0.05	−0.11	0.04	0.01	0.01	−0.22	0.01	0.03	0.04	−0.07	0.03	−0.02	0.00
Mid-frontal → face-responsive	−0.05	0.02	0.01	0.00	0.03	−0.01	0.00	0.00	−0.32	−0.03	0.02	0.08	−0.01	0.04	0.04	−0.02	0.04	0.00	−0.01	0.02
Mid-frontal → sup. parietal	0.00	–	–	–	0.01	–	–	–	0.03	–	–	–	0.02	–	–	–	0.02	–	–	–

We report the intrinsic connections, which refer to the impact that one region exerts over another in the absence of experimental perturbation and the bilinear terms, which refer to the influence of house-, face- and chair-stimuli on the intrinsic connections. Int. con., intrinsic connection. H > C & F indicates greater connectivity during the perception of houses relative to chairs and faces; F > H & C indicates greater connectivity during the perception of faces relative to houses and chairs; and C > H & F indicates greater connectivity during the perception of chairs relative to houses and faces. Connectivity parameters >0 with 95% confidence are reported in bold. The forward connections from inferior occipital cortex to the house, face and chair-responsive regions are strongest during the presentation of house-, face- and chair-stimuli, respectively. In contrast, the backward and forward connections between prefrontal cortex, superior parietal cortex and the category responsive regions do not appear to be stimulus-sensitive. It should be noted that subject 3 did not show an effect of house > faces & chairs and therefore the connectivity parameters were estimated for the face- and chair-responsive regions only. Confidence intervals are reported in Table 3.

prefrontal cortex in all five subjects. Thus, the intrinsic connectivity from prefrontal cortex to the 'house-responsive' region was stronger during visual imagery of houses than any other category; the intrinsic connectivity from prefrontal cortex to the 'face-responsive' region was strongest during visual imagery of faces; and the intrinsic connectivity from prefrontal cortex to the 'chair-responsive' region was strongest during visual imagery of chairs. In contrast, content-related activation in occipito-temporal cortex was not mediated by increased connectivity from the precuneus or superior parietal cortex. Thus, the intrinsic connectivity between the precuneus, superior parietal cortex and the category responsive regions was similar during visual imagery of chairs, faces and houses (see Tables 4 and 5). These results are consistent with our prediction that content-related activation during visual imagery is mediated by top-down mechanisms.

Discussion

In the present study, we examined the neuronal interactions that mediate content-related activation in occipito-temporal cortex during visual perception and visual imagery. Our investigation was motivated by the idea that content-related activation is not an intrinsic property of a cortical area but, rather, depends on both forward and backward connections (Damasio, 1989; Mesulam, 1990; Fuster, 1997; McIntosh, 2000; Friston and Price, 2001). We found that category-specific activation during visual perception was associated with increased effective connectivity from early visual cortex. In particular, the effective connectivity from inferior occipital cortex to the 'house-responsive' regions was stronger during the presentation of house stimuli than any other category. Similarly, the connectivity from inferior occipital cortex to the 'face-responsive' regions was strongest during the perception of faces. Finally, the connectivity from inferior occipital cortex to the 'chair-responsive' regions was strongest during the presentation of chair stimuli. This bottom-up mediation replicates and extends our previous study, with an independent group of five subjects (Mechelli *et al.*, 2003).

In contrast, content-related activation during visual imagery was associated with increased effective connectivity from prefrontal cortex. Thus, the connectivity from prefrontal cortex to the 'house-responsive' regions was stronger during

Table 3

Confidence intervals for the connectivity parameters during visual perception

Visual perception	Subject 1				Subject 2				Subject 3				Subject 4				Subject 5			
	Int. con.	H > C&F	C > H&F	F > H&C	Int. con.	H > C&F	C > H&F	F > H&C	Int. con.	H > C&F	C > H&F	F > H&C	Int. con.	H > C&F	C > H&F	F > H&C	Int. con.	H > C&F	C > H&F	F > H&C
Forward connections																				
Inf. occipital → house-responsive	**0.11**	**0.12**	0.16	0.12	**0.13**	**0.15**	0.14	0.11	–	–	–	–	**0.17**	**0.12**	0.18	0.16	0.14	**0.12**	0.13	0.08
Inf. occipital → chair-responsive	**0.11**	0.13	**0.12**	0.12	**0.14**	0.17	**0.11**	0.14	**0.12**	0.14	**0.13**	0.16	**0.19**	0.16	**0.17**	0.17	**0.18**	0.10	**0.16**	0.10
Inf. occipital → face-responsive	**0.16**	0.17	0.17	**0.11**	0.15	0.10	0.17	**0.10**	0.11	0.13	0.12	**0.19**	**0.18**	0.16	0.13	**0.18**	**0.16**	0.12	0.17	**0.15**
House-responsive → sup. parietal	0.16	0.11	0.13	0.11	**0.18**	0.10	0.13	0.12	–	–	–	–	**0.17**	0.10	0.13	0.19	**0.16**	0.10	0.18	0.11
Chair-responsive → sup. parietal	**0.12**	0.15	0.15	0.12	0.19	0.10	0.13	0.11	0.11	0.14	0.13	0.20	**0.19**	0.16	0.16	0.14	**0.17**	0.11	0.15	0.11
Face-responsive → sup. parietal	**0.13**	0.14	0.13	0.14	0.14	0.09	0.11	0.11	**0.19**	0.15	0.14	0.11	**0.18**	0.12	0.12	0.11	**0.18**	0.12	0.16	0.18
House-responsive → mid-frontal	0.12	0.12	0.17	0.17	0.14	0.09	0.13	0.15	–	–	–	–	0.11	0.11	0.11	0.11	0.10	0.11	0.10	0.12
Chair-responsive → mid-frontal	0.16	0.17	0.12	0.18	0.15	0.08	0.08	0.14	0.16	0.14	0.10	0.10	0.12	0.11	0.11	0.11	0.10	0.12	0.11	0.10
Face-responsive → mid-frontal	0.14	0.14	0.16	0.13	0.13	0.08	0.08	0.15	0.12	0.18	0.13	0.10	0.11	0.11	0.13	0.11	0.09	0.09	0.10	0.08
Sup. parietal → mid-frontal	0.18	–	–	–	0.14	–	–	–	0.13	–	–	–	0.11	–	–	–	0.08	–	–	–
Backward connections																				
House-responsive → inf. occipital	**0.13**	0.16	0.15	0.14	**0.17**	0.15	0.17	0.13	–	–	–	–	**0.11**	0.17	0.17	0.19	**0.16**	0.17	0.19	0.18
Chair-responsive → inf. occipital	**0.14**	0.15	0.14	0.13	0.12	0.14	0.14	0.13	**0.19**	0.11	0.12	0.10	0.12	0.11	0.18	0.17	**0.12**	0.16	0.13	0.14
Face-responsive → inf. occipital	**0.15**	0.12	0.13	0.14	**0.17**	0.18	0.18	0.14	**0.12**	0.10	0.14	0.10	0.14	0.12	0.16	0.16	**0.13**	0.15	0.14	0.14
Sup. parietal → house-responsive	0.17	0.13	0.12	0.14	**0.10**	0.15	0.17	0.13	–	–	–	–	**0.11**	0.12	0.11	0.14	0.10	0.14	0.13	0.16
Sup. parietal → chair-responsive	**0.14**	0.13	0.12	0.12	0.16	0.15	0.12	0.11	0.12	0.13	0.14	0.10	**0.12**	0.11	0.12	0.13	**0.16**	0.16	0.16	0.15
Sup. parietal → face-responsive	**0.13**	0.16	0.16	0.18	0.16	0.12	0.11	0.13	0.12	0.14	0.12	0.10	0.14	0.11	0.12	0.16	0.10	0.13	0.12	0.16
Mid-frontal → house-responsive	0.16	0.18	0.15	0.14	0.16	0.13	0.10	0.12	–	–	–	–	0.13	0.11	0.14	0.11	0.08	0.17	0.14	0.14
Mid-frontal → chair-responsive	0.16	0.19	0.17	0.11	0.18	0.13	0.13	0.12	0.13	0.14	0.11	0.10	0.12	0.11	0.11	0.12	0.11	0.10	0.11	0.10
Mid-frontal → face-responsive	0.15	0.18	0.13	0.14	0.19	0.12	0.11	0.11	0.17	0.18	0.10	0.09	0.12	0.12	0.11	0.12	0.12	0.09	0.09	0.09
Mid-frontal → sup. parietal	0.17	–	–	–	0.13	–	–	–	0.14	–	–	–	0.13	–	–	–	0.13	–	–	–

It can be noticed that there was a high degree of consistency in these confidence intervals. For instance, all fell within a similar range: 0.11–0.19 (subject 1), 0.08–0.19 (subject 2), 0.10–0.19 (subject 3), 0.10–0.19 (subject 4), 0.08–0.19 (subject 5). The confidence intervals for those connectivity parameters >0 with 95% confidence are reported in bold. Int. con., intrinsic connection.

visual imagery of houses than any other category; the connectivity from prefrontal cortex to the 'face-responsive' regions was strongest during visual imagery of faces; and the connectivity from prefrontal cortex to the 'chair-responsive' regions was strongest during visual imagery of chairs. Although previously hypothesized, this top-down mediation of category-related responses could not be demonstrated with conventional analyses of fMRI activations (e.g. Ishai *et al.*, 2000b).

Our findings indicate that category-specific patterns of activation observed during visual perception and visual imagery are mediated by bottom-up and top-down mechanisms, respectively. These differential neuronal interactions are likely to reflect different cognitive strategies adopted by subjects during perception and imagery. While attentively viewing pictures of faces, houses and chairs, subjects were not required to engage cognitive resources. Thus, the retrieval of sensory representations, established in the ventral occipito-temporal cortex, was driven by bottom-up, perceptual processes that originated in early visual areas. Conversely, during visual imagery, subjects were required to generate vivid mental images of familiar houses, faces and chairs from long-term memory. Thus, in the absence of retinal input, sensory representations were reactivated by top-down, cognitive processes that originated in parietal and frontal cortex. The patterns of differential connectivity revealed with our analysis are therefore consistent with a task analysis from a cognitive perspective.

Our study also demonstrates that, although prefrontal and superior parietal cortices are associated with similar patterns of activations during visual imagery of houses, faces and chairs, these regions can be functionally segregated on the basis of their differential neuronal interactions. Interestingly, we did not detect category-selective patterns of activation within prefrontal and superior parietal regions, even with lower statistical thresholds. Yet when the coupling between these regions and the category-responsive areas in occipito-temporal cortex was examined, two distinct patterns of connectivity were identified consistently across subjects. The backward connections from prefrontal cortex to the house-, face- and chair-responsive regions were strongest during visual imagery of houses, faces and chairs, respectively. In contrast, the backward connections from superior parietal cortex to the house- faces- and chair-responsive regions were not stimulus-sensitive and were similar during visual imagery of houses, faces and chairs. This dissociation indicates distinct roles of prefrontal and superior parietal areas during visual imagery.

We have previously argued that the fronto-parietal network mediates the retrieval of pictorial representations stored in long-term memory and their maintenance through visual imagery (Ishai *et al.*, 2000b). On the basis of our connectivity analysis, we suggest that this 'imagery network' is composed of a general attentional mechanism arising in parietal cortex and a content-sensitive mechanism originated in prefrontal cortex.

Table 4

Subject-specific connectivity parameters during visual imagery, as identified by dynamic causal modelling

Visual imagery	Subject 1				Subject 2				Subject 3				Subject 4				Subject 5			
	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C
Forward connections																				
Precuneus → house-responsive	0.13	0.01	0.00	0.00	**0.21**	0.01	0.10	−0.02	–	–	–	–	**0.34**	0.01	0.00	0.00	0.11	−0.01	0.00	−0.04
Precuneus → chair-responsive	**0.26**	0.02	−0.04	0.02	−0.11	0.04	0.06	0.01	**0.32**	0.00	0.00	0.00	0.03	−0.11	0.06	0.01	**0.32**	−0.19	0.03	0.01
Precuneus → face-responsive	**0.32**	−0.04	−0.01	0.01	**0.29**	0.02	−0.04	0.02	**0.28**	0.00	−0.01	0.00	**0.24**	−0.07	0.00	0.03	**0.19**	0.00	0.00	0.02
House-responsive → sup. parietal	0.02	0.00	0.00	0.00	−0.09	−0.07	−0.02	0.04	–	–	–	–	0.05	0.00	0.00	0.00	**0.53**	−0.01	0.01	0.02
Chair-responsive → sup. parietal	**0.55**	−0.04	0.01	0.01	**0.23**	0.07	−0.03	−0.03	**0.28**	0.04	−0.05	0.00	**0.23**	0.03	−0.27	0.09	0.03	0.01	0.00	−0.01
Face-responsive → sup. parietal	−0.01	−0.02	0.02	0.00	0.17	0.06	−0.02	0.01	−0.18	−0.07	−0.01	0.00	0.09	0.01	0.00	0.00	−0.11	0.09	−0.09	−0.02
House-responsive → mid-frontal	0.04	−0.01	0.00	0.00	−0.59	0.00	−0.01	0.00	–	–	–	–	0.04	0.07	0.00	0.11	0.01	−0.02	0.00	0.01
Chair-responsive → mid-frontal	0.06	−0.04	0.01	0.01	0.11	0.00	0.01	0.00	0.08	0.00	−0.01	0.00	0.10	0.06	0.00	0.03	0.04	0.00	−0.02	−0.01
Face-responsive → mid-frontal	−0.07	0.00	0.00	0.00	0.13	0.01	0.04	−0.01	−0.13	−0.05	−0.01	0.01	−0.13	−0.10	0.01	0.06	0.06	0.02	−0.01	−0.09
Sup. parietal → mid-frontal	0.00	–	–	–	0.00	–	–	–	−0.01	–	–	–	0.02	–	–	–	−0.04	–	–	–
Backward connections																				
House-responsive → precuneus	**0.30**	0.01	0.05	−0.13	**0.33**	0.06	0.06	0.02	–	–	–	–	0.04	0.04	0.04	0.00	−0.05	0.03	−0.15	−0.28
Chair-responsive → precuneus	0.11	0.03	−0.05	0.06	**0.20**	−0.02	0.00	0.00	0.11	0.00	0.00	0.00	**0.27**	−0.11	0.04	0.00	**0.22**	0.04	0.11	−0.07
Face-responsive → precuneus	**0.20**	−0.04	−0.06	0.00	−0.13	0.06	0.00	0.00	**0.24**	−0.04	−0.07	0.11	−0.37	0.12	−0.22	−0.07	**0.64**	−0.37	0.11	0.16
Sup. parietal → house-responsive	**0.34**	0.11	0.00	0.02	−0.32	−0.03	0.05	0.02	–	–	–	–	**0.31**	0.06	0.03	0.00	−0.04	0.03	−0.23	−0.03
Sup. parietal → chair-responsive	**0.20**	−0.07	−0.07	0.11	0.11	0.10	0.00	0.01	**0.39**	0.03	0.04	0.01	0.09	−0.11	0.01	0.05	0.12	0.06	0.04	−0.12
Sup. parietal → face-responsive	−0.41	−0.15	−0.04	0.05	**0.20**	−0.06	0.00	0.01	**0.58**	−0.34	−0.11	0.00	0.04	0.03	0.00	0.00	−0.04	−0.05	0.01	0.02
Mid-frontal → house-responsive	0.01	**0.49**	0.06	−0.44	−0.11	**0.20**	0.00	0.06	–	–	–	–	−0.64	**0.24**	−0.34	0.16	−0.36	**0.21**	−0.44	−0.17
Mid-frontal → chair-responsive	−0.09	−0.12	**0.22**	−0.19	−0.22	0.04	**0.34**	−0.06	0.08	−0.03	**0.25**	0.10	−0.05	−0.36	**0.56**	0.12	−0.09	0.01	**0.33**	−0.13
Mid-frontal → face-responsive	−0.32	−0.22	−0.06	0.16	−0.47	−0.36	−0.02	**0.26**	−0.22	−0.13	0.02	**0.28**	−0.14	0.07	−0.44	**0.22**	−0.76	−0.11	−0.21	**0.66**
Mid-frontal → sup. parietal	0.02	–	–	–	0.06	–	–	–	0.01	–	–	–	0.02	–	–	–	−0.01	–	–	–

We report the intrinsic connections, which refer to the impact that one region exerts over another in the absence of experimental perturbation and the bilinear terms, which refer to the influence of house-, chair- and face-stimuli on the intrinsic connections. Int. con., intrinsic connectionH> C & F indicates greater connectivity during the imagery of houses relative to chairs and faces; F> H & C indicates greater connectivity during the imagery of faces relative to houses and chairs; and C> H & F indicates greater connectivity during the imagery of chairs relative to houses and faces. Connectivity parameters >0 with 95% confidence are reported in bold. The backward connections from prefrontal cortex to the house-, face- and chair-responsive regions are strongest during the imagery of houses, faces and chairs respectively. In contrast, the backward and forward connections between the precuneus, superior parietal cortex and the category responsive regions do not appear to be stimulus-sensitive. It should be noted that subject 3 did not show an effect of house> faces & chairs and therefore the connectivity parameters were estimated for the face- and chair-responsive regions only.

Numerous studies of spatial and non-spatial attention tasks have shown activation in parietal cortex (e.g. Corbetta *et al.*, 1998; Kastner *et al.*, 1999; Wojciulik and Kanwisher, 1999). Moreover, parietal activation has been reported in a variety of mental imagery tasks (e.g. Mellet *et al.*, 2000; Ishai *et al.*, 2002). It is therefore reasonable to assume that superior parietal cortex mediates the attentional processes required to perform the imagery task, irrespective of stimulus-content. In contrast, several electrophysiological and lesion studies have shown that the prefrontal cortex is crucial for object recognition (e.g. Bachevalier and Mishkin, 1986; Wilson *et al.*, 1993; Parker *et al.*, 1998). Moreover, recent studies have revealed the existence of category-selective responses in the monkey prefrontal cortex (Freedman *et al.*, 2001). A similar specialization, although undetected with conventional analyses of fMRI activations, may also exist in the human brain. Indeed, our study suggests that prefrontal areas mediate the actual retrieval of sensory representations which are established in the ventral occipito-temporal cortex.

Interestingly, the pattern of activation in the precuneus was remarkably similar to that in the superior parietal cortex. The precuneus showed greater activation during imagery relative to imagery-control, but did not express any category-selective patterns of activation. Furthermore, the backward and forward connections from the precuneus to the category-responsive regions in the occipito-temporal cortex were similar during visual imagery of all categories, namely houses, faces and chairs. Previous studies have shown that the precuneus was implicated in retrieval from episodic memory, irrespective of modality or format, e.g. during picture recall and auditory word recall (see Buckner *et al.*, 1996). Moreover, the precuneus was activated in numerous imagery studies, irrespective of the content (Fletcher *et al.*, 1995; Mellet *et al.*, 1998; Ishai *et al.*, 2000b, 2002). The pattern of intrinsic connectivity revealed by our DCM analysis supports the view that the precuneus has a general role in retrieval from episodic memory and during memory-related imagery.

Our findings are consistent with current neurophysiological models of visual working memory developed in the context of single-unit recording studies in behaving monkeys (Fuster and Bauer, 1974; Miller *et al.*, 1996) and supported by recent functional imaging studies in humans (Druzgal and D'Esposito, 2003). These models predict that visual working memory is mediated by neuronal interactions between prefrontal and

Table 5

Confidence intervals for the connectivity parameters during visual imagery

Visual imagery	Subject 1				Subject 2				Subject 3				Subject 4				Subject 5			
	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C	Int. con.	H > C & F	C > H & F	F > H & C
Forward connections																				
Precuneus → house-responsive	0.17	0.09	0.10	0.10	**0.12**	0.12	0.12	0.12	–	–	–	–	**0.18**	0.10	0.11	0.10	0.13	0.11	0.11	0.12
Precuneus → chair-responsive	**0.14**	0.11	0.11	0.11	0.13	0.12	0.12	0.12	**0.12**	0.12	0.13	0.14	0.17	0.13	0.11	0.11	**0.12**	0.12	0.13	0.11
Precuneus → face-responsive	**0.15**	0.10	0.10	0.11	**0.16**	0.12	0.13	0.12	**0.12**	0.14	0.12	0.12	**0.19**	0.11	0.12	0.11	**0.11**	0.11	0.12	0.12
House-responsive → sup. parietal	0.15	0.10	0.13	0.12	0.14	0.14	0.12	0.13	–	–	–	–	0.16	0.10	0.11	0.10	**0.15**	0.15	0.11	0.11
Chair-responsive → sup. parietal	**0.18**	0.11	0.12	0.13	**0.12**	0.12	0.13	0.12	**0.13**	0.16	0.12	0.12	**0.16**	0.10	0.17	0.10	0.15	0.11	0.11	0.11
Face-responsive → sup. parietal	0.14	0.09	0.09	0.10	0.18	0.12	0.12	0.12	0.16	0.15	0.13	0.13	0.18	0.10	0.12	0.11	0.17	0.12	0.14	0.11
House-responsive → mid-frontal	0.15	0.11	0.10	0.09	0.19	0.12	0.12	0.13	–	–	–	–	0.17	0.12	0.12	0.13	0.14	0.12	0.12	0.11
Chair-responsive → mid-frontal	0.15	0.11	0.11	0.11	0.12	0.12	0.13	0.12	0.19	0.12	0.13	0.14	0.17	0.11	0.11	0.11	0.14	0.11	0.12	0.11
Face-responsive → mid-frontal	0.17	0.10	0.09	0.09	0.15	0.12	0.13	0.12	0.20	0.13	0.14	0.16	0.18	0.11	0.11	0.12	0.15	0.12	0.13	0.12
Sup. parietal → mid-frontal	0.10	–	–	–	0.12	–	–	–	0.12	–	–	–	0.13	–	–	–	0.12	–	–	–
Backward connections																				
House-responsive → precuneus	**0.09**	0.11	0.13	0.14	**0.19**	0.12	0.13	0.12	–	–	–	–	0.17	0.11	0.11	0.10	0.13	0.13	0.15	0.11
Chair-responsive → precuneus	0.18	0.12	0.11	0.13	**0.15**	0.12	0.13	0.13	0.13	0.12	0.12	0.12	**0.16**	0.10	0.12	0.10	**0.12**	0.13	0.11	0.13
Face-responsive → precuneus	**0.10**	0.13	0.12	0.12	0.16	0.13	0.12	0.12	**0.12**	0.14	0.12	0.12	0.17	0.11	0.12	0.12	**0.14**	0.19	0.16	0.17
Sup. parietal → house-responsive	**0.11**	0.12	0.12	0.14	0.19	0.14	0.13	0.12	–	–	–	–	**0.16**	0.11	0.12	0.11	0.12	0.13	0.17	0.14
Sup. parietal → chair-responsive	**0.11**	0.11	0.14	0.13	0.18	0.13	0.13	0.12	**0.12**	0.14	0.12	0.12	0.17	0.11	0.11	0.11	0.16	0.12	0.13	0.14
Sup. parietal → face-responsive	0.17	0.18	0.16	0.17	**0.16**	0.12	0.12	0.13	**0.14**	0.17	0.12	0.12	0.17	0.11	0.10	0.10	0.15	0.12	0.11	0.12
Mid-frontal → house-responsive	0.16	**0.09**	0.11	0.18	0.18	**0.13**	0.12	0.13	–	–	–	–	0.18	**0.12**	0.10	0.16	0.15	**0.16**	0.18	0.15
Mid-frontal → chair-responsive	0.15	0.14	**0.13**	0.16	0.19	0.14	**0.13**	0.12	0.13	0.14	**0.12**	0.13	0.17	0.18	**0.19**	0.17	0.18	0.13	**0.13**	0.13
Mid-frontal → face-responsive	0.18	0.14	0.13	0.14	0.19	0.13	0.12	**0.12**	0.12	0.15	0.13	**0.14**	0.18	0.14	0.18	**0.13**	0.19	0.17	0.17	**0.18**
Mid-frontal → sup. parietal	0.11	–	–	–	0.13	–	–	–	0.12	–	–	–	0.14	–	–	–	0.12	–	–	–

It can be noticed that there was a high degree of consistency in these confidence intervals. For instance, all fell within a similar range: 0.09–0.18 (subject 1), 0.12–0.19 (subject 2), 0.12–0.20 (subject 3), 0.10–0.19 (subject 4), 0.11–0.19 (subject 5). The confidence intervals for those connectivity parameters >0 with 95% confidence are reported in bold. Int. con., intrinsic connection.

occipito-temporal cortices. For instance, the retrieval of visual information may be mediated by a top-down flow of information from prefrontal cortex to content-sensitive regions in the ventral stream. Indeed, during a delayed recognition task with face objects, activation increased parametrically with memory load in the prefrontal cortex and the 'fusiform face area' (Druzgal and D'Esposito, 2003). Similarly, in our study, the content-specific imagery effects in the ventral stream were mediated by top-down mechanisms arising in mid-frontal cortex.

In summary, our effective connectivity analysis revealed distinct neuronal mechanisms that mediate content-related activity in the human brain, during visual perception and visual imagery respectively. The modulation of these neuronal mechanisms by task, stimulus and presentation format is of particular interest. It has been shown that activation in prefrontal cortex is negligible when pictures of objects are presented in a slow-paced single-trial format, but is more pronounced when pictures are masked and briefly presented (Bar *et al.*, 2001). It therefore seems that prefrontal cortex may mediate content-related activity during visual perception, but only under experimental conditions that explicitly invoke top-down processing. Future studies will address the nature of the interactions between bottom-up and top-down processes and their modulation by the experimental paradigm.

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