Effective Connectivity within the Distributed Cortical Network for Face Perception

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Face perception elicits activation within a distributed cortical network in the human brain. The network includes visual ("core") regions, as well as limbic and prefrontal ("extended") regions, which process invariant facial features and changeable aspects of faces, respectively. We used functional Magnetic Resonance Imaging and Dynamic Causal Modeling to investigate effective connectivity and functional organization between and within the core and the extended systems. We predicted a ventral rather than dorsal connection between the core and the extended systems during face viewing and tested whether valence and fame would alter functional coupling within the network. We found that the core system is hierarchically organized in a predominantly feed-forward fashion, and that the fusiform gyrus (FG) exerts the dominant influence on the extended system. Moreover, emotional faces increased the coupling between the FG and the amygdala, whereas famous faces increased the coupling between the FG and the orbitofrontal cortex. Our results demonstrate content-specific dynamic alterations in the functional coupling between visual-limbic and visual-prefrontal face-responsive pathways.

Keywords: cortical network, dynamic causal modeling, faces, fMRI, neuronal interaction

Introduction

Face perception, a highly developed visual skill in humans, is mediated by activation in a distributed neural system that encompasses visual, limbic, and prefrontal regions (Haxby et al. 2000; Ishai et al. 2005). The cortical network that mediates face perception includes the fusiform gyrus (FG), an extrastriate region that processes the identification of individuals (Kanwisher et al. 1997; Ishai et al. 1999; Grill-Spector et al. 2004); the superior temporal sulcus (STS), where gaze direction and speech-related movements are processed (Hoffman and Haxby 2000; Puce et al. 2003); the amygdala (AMG) and insula, where facial expressions are processed (Breiter et al. 1996; Morris et al. 1996; Phillips et al. 1997; Ishai et al. 2004); the inferior frontal gyrus (IFG), where semantic aspects are processed (Leveroni et al. 2000; Ishai et al. 2002); and regions of the reward circuitry, including the nucleus accumbens and orbitofrontal cortex (OFC), where facial beauty and sexual relevance are assessed (Aharon et al. 2001; O'Doherty et al. 2003; Ishai 2007; Kranz and Ishai 2006). It has been proposed that the cortical network for face perception can be divided into a "core" system that includes the inferior occipital gyrus (IOG), FG, and STS, and an extended system that includes the AMG, insula, IFG, and OFC (Haxby et al. 2000, 2002). It is currently unknown whether the core and the extended systems indeed comprise a cortical network and how these regions are functionally connected.

To investigate effective connectivity within the distributed cortical network for face perception, we combined conventional Statistical Parametric Mapping (SPM) with Dynamic Causal Modeling (DCM), a new analytic approach that allows the assessment of effective connectivity within cortical networks (Friston et al. 2003). DCM yields a measure of cortical connectivity that is directional, based on interactions modeled at the neuronal level, and independent of coincidental stimulus-locked coupling (Friston et al. 2003; Penny et al. 2004a). DCM has been previously employed to investigate category-selective effects (Mechelli et al. 2003; Noppeney et al. 2006); bottom-up and top-down coupling during perception and imagery (Mechelli et al. 2004); stimulus visibility (Haynes et al. 2005); effective connectivity during spelling and rhyming (Bitan et al. 2005); and AMG–hippocampal coupling during memory retrieval (Smith et al. 2006).

We used DCM and Bayesian model selection to investigate the pattern of interactions within a network of face-selective regions during the perception of various face stimuli. We addressed the following issues: 1) What is the architecture of the core system? Is it predominantly a feed-forward architecture, a recurrent architecture, or is it organized in parallel? 2) How does the core system interact with the extended system? We hypothesized that during attentive viewing, due to the pivotal role of the FG in face perception, the ventral, but not the dorsal regions of the core system would exert influence on the extended system. 3) Are there any differences in the patterns of effective connectivity between the left and the right hemisphere? 4) Can functional specialization be explained in terms of selective enabling of coupling between regions? We hypothesized that valence and fame would differentially alter effective connectivity between the core and the extended systems, namely that emotional faces would increase effective connectivity between the FG and the AMG, whereas famous faces would increase the connectivity between the FG and the OFC.

Methods

Subjects

Ten healthy subjects (5 males, mean age 25 years) with normal vision participated in the study. All subjects gave written informed consent in accordance with protocols approved by the University Hospital of Zurich.

Stimuli and Task

Subjects were presented with 4 types of face stimuli: black and white line drawings of unfamiliar faces, and gray scale photographs of unfamiliar, famous, and emotional (fearful and happy) faces. Phase scrambled versions of these faces were used as visual baseline (see Ishai et al. 2005). Each stimulus was presented for 3 s. Each run included 3 alternating epochs of scrambled faces (24 s) and faces (36 s). Five runs

(line drawings, famous, emotional, and 2 runs with unfamiliar faces) were collected for each subject and the order of stimulus formats was randomized. Stimuli were generated using Presentation (www.neurobs.com, version 9.13) and were projected with a magnetically shielded LCD video projector onto a translucent screen. The subject was instructed to attentively view the faces.

Data Acquisition

Data were collected using a 3-T Philips Intera whole body MR scanner. Functional data were obtained from 39 transverse slices covering the whole brain with a spatial resolution of 2.3 mm × 2.3 mm × 3 mm (acquisition matrix 96 × 96), using a sensitivity-encoded singleshot gradient-echo planar sequence. Images were acquired with fields of view = 220 mm, time repetition (TR) = 3000 ms, time echo (TE) = 35 ms, θ = 82°, and with a SENSE acceleration factor of 2.0 (Pruessmann et al. 1999). High-resolution spoiled gradient recalled echo structural images were obtained with 1 mm × 1 mm × 1 mm spatial resolution (acquisition matrix 224 × 224), TE = 2.30 ms, TR = 20 ms, θ = 20°. These T_1-weighted images provided detailed anatomical information for the region of interest (ROI) analysis.

Data Analysis

Preprocessing

Data were analyzed using SPM5 software (www.fil.ion.ucl.ac.uk/spm/). All volumes were slice time corrected, realigned to the first volume, corrected for motion artifacts, mean-adjusted by proportional scaling, normalized into standard stereotactic space (template provided by the Montreal Neurological Institute), and smoothed using a 5-mm full-width at half-maximum Gaussian kernel. The time series were high-pass filtered to eliminate low-frequency components (filter width 128 s) and adjusted for systematic differences across trials.

Statistical Parametric Mapping

The analysis was based on a conventional general linear model (Friston, Holmes, Poline, et al. 1995; Friston, Holmes, Worsley, et al. 1995) using 3 regressors, representing the 3 experimental effects: all faces versus scrambled faces; emotional faces versus scrambled faces; and famous faces versus scrambled faces. The main effect of faces was used for ROI selection and time series extraction: A set of ROIs was independently defined for each subject, which included the IOG, FG, STS, AMG, IFG, and the OFC. The anatomical locations of these clusters were determined by superimposing the statistical maps on the coplanar high-resolution structural images. Regional responses were defined as the average of face-responsive voxels within a 6-mm radius centered on the maximum voxel. The significance threshold was set to $P < 0.001$.

Dynamic Causal Modeling

The hemodynamic model used by DCM has been biophysically validated (Friston et al. 2003; Stephan et al. 2004), however, the neural model is experiment dependent and requires specific hypotheses. Thus, the brain regions included in the model, the anatomical connectivity between them and the modulation by experimental conditions have to be specified (Penny et al. 2004b). The first regressor, the main effect of faces, was used as a direct or driving input that entered the IOG, such that any regional connections, present in the tested models, mediate the propagation of face-selective responses in the IOG around the face-system. The second and third effects (valence and fame) were used as bilinear modulators of connectivity to assess the selective enabling of pathways by these factors. Model fitting was achieved by adjusting the connection parameters, such that the activity predicted in each region most closely matched that observed in the actual data (Friston et al. 2003). The parameters optimize a variational free-energy bound on the models evidence. This ensures that the model fit uses the free parameters in a parsimonious way. After model inversion the free energy can be used as an approximation to the model evidence, namely the probability of the data given the model. This quantity is used below to compare different models using Bayes factors.

Model Comparisons

Our analysis was based on Bayesian model comparison using Bayes factors to select among competing models. The models we explored were based upon the theoretical division into core and extended systems (Haxby et al. 2000, 2002). Models were contrasted based on their ability to explain the observed data, in terms of their evidence. This is probability of the data from the ith subjects data given the jth model: $p(y_i|m_j)$. Using a Bayesian framework, successive pairwise comparisons were made between models. Two criteria were used to assess the evidence in favor of one model versus another, namely the Bayesian and Akaike's Information Criteria (Penny et al. 2004b). The former is biased toward simple models, whereas the latter is biased toward complex models (Kass and Raftery 1993). Both are approximations to $B_{jk}^{(i)} = p(y_i|m_j)/p(y_i|m_k)$, which is the probability of the ith subjects data, given the jth model, relative to the kth model. To ensure a consistent inference about models, the Bayes factors reported here (and used in any statistical tests) reflect the smaller of these 2 values and are therefore conservative estimates. We report the Bayes factors pooled over all subjects in terms of each subject-specific Bayes factor $B_{jk} = \prod_i B_{jk}^{(i)} = p(y_1, \ldots, y_n|m_j)/p(y_1, \ldots, y_n|m_k)$ for n subjects. This is effectively the relative evidence for each model using the data from all subjects ($y_1, \ldots, y_n$). To ensure this model comparison was not unduly affected by one subject, we also tested the consistency of the Bayes factor for each subject using a χ^2-test on the proportion of subjects favoring a particular model (i.e., $B_{jk}^{(i)} > 1$).

Testing Bilinear Effects of Valence and Fame

The enabling effects of emotion and fame on specific connections were assessed using classical parametric tests (t-tests) on the conditional expectation of the bilinear effect from each subject. Coupling strengths in dynamic models play the same role as rate constants in kinetic models. In other words, they are measured in units of per second. Thus, a modulatory or enabling effect of 0.24, given a regional coupling of 0.48, represents a 50% increase in connectivity. We therefore report in the Tables both the increase in coupling (rate) and its percent increase, relative to the underlying regional coupling. As can be seen, the selective enabling of specific connections can be quite profound, in proportional terms.

Results

The main effect of faces (as compared with scrambled faces) revealed activation within a distributed cortical network that included visual, limbic, and prefrontal regions (Fig. 1 and Table 1). The DCM analysis included 3 regions representing the core system (the IOG, FG, and STS) and 3 regions (the AMG, IFG, and OFC) representing the extended system.

The Core System

Directional Connectivity within the Right Hemisphere Core System

Bayesian model selection was used to determine the best model of effective connectivity within the core system. To determine the most probable pattern of effective connectivity, models were divided into 6 prototypes (Fig. 2A). Within each prototype, the backwards connectivity was varied systematically, creating 24 models from these 6 prototypes. We found greater evidence in favor of a direct and separate influence of the IOG on the FG and STS, than any other model (Fig. 2A, Prototype 2). The values in Supplementary Table 1 reflect evidence at the level comparable to classic fixed effects analysis, namely the relative probability of data from all subjects given a particular model. A Bayes Factor (B) greater than the natural exponent e ($B > 2.718$) provides strong evidence in favor of one model (Penny et al. 2004b). Thus, the feed-forward variant of Prototype 2 (Supplementary Table 1: shaded row) was favored ($B = 3.1$) over the next best 3-tier model (Prototype 1). Greater evidence for this model ($B > 1$) was observed in 9 out of 10 subjects, when considered separately ($\chi^2 = 6.4$, $P < 0.011$). Evidence against
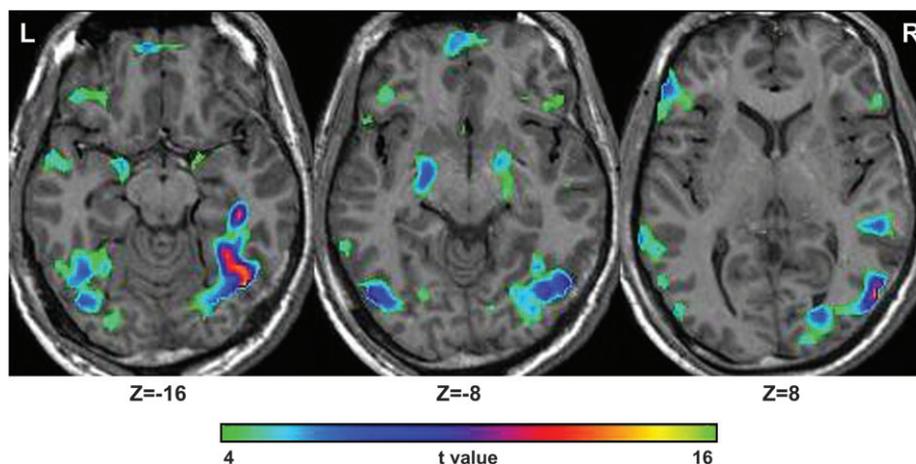
Figure 1. Face perception elicits activation within a distributed cortical network. Axial sections, taken from a representative subject, illustrate activation within the core (IOG, FG, STS) and extended (AMG, IFG, OFC) systems. Coordinates are in the Talaraich space. L = left, R = right.

Table 1
A network of face-selective regions

Region	N	Mean coordinates		
		x	y	z
L. IOG	10	−43(1)	−76(1)	−3(1)
R. IOG	10	41(2)	−77(1)	−1(1)
L.FG	10	−41(1)	−56(1)	−13(1)
R.FG	10	38(1)	−57(2)	−13(1)
L.STS	7	−55(2)	−54(3)	11(3)
R.STS	10	48(2)	−48(3)	10(2)
L.AMG	6	−19(2)	−4(1)	−13(1)
R.AMG	8	18(1)	−7(1)	−12(1)
L.IFG	5	−49(3)	18(4)	14(5)
R.IFG	7	50(1)	27(2)	10(2)
M.OFC	7	−3(3)	55(3)	−18(2)

Note: N indicates number of subjects who showed significant activation in each region. Coordinates are in the normalized space of the brain atlas (Talairach and Tournoux 1998). Standard error of the means are indicated in parentheses. L = left, R = right, M = medial.

the role of interconnectivity between FG and STS in terms of Prototypes 4 and 5 was present but weak when data from all subjects were considered. However, when these data were considered for each subject separately (in terms of the most likely model), there was reliable evidence in favor of feed-forward Prototype 2 in comparison to either Prototype 4 (χ^2 = 6.4, $P < 0.011$) or Prototype 5 (χ^2 = 6.4, $P < 0.011$). The weight of evidence in favor of a feed-forward system was not increased by including backwards connections (see Supplementary Table 1). In other words, the extra complexity induced by adding backward connections was not offset by increased model fit (Penny et al. 2004b). Taken together, these results suggest that the IOG directly influences both the FG and STS with little evidence of feedback or collateral influences on the observed blood oxygen level–dependent response.

Functionally Selective Coupling within the Right Hemisphere Core System

The effects of valence and fame were introduced to the DCM as bilinear terms (see Methods). Group statistics for the bilinear
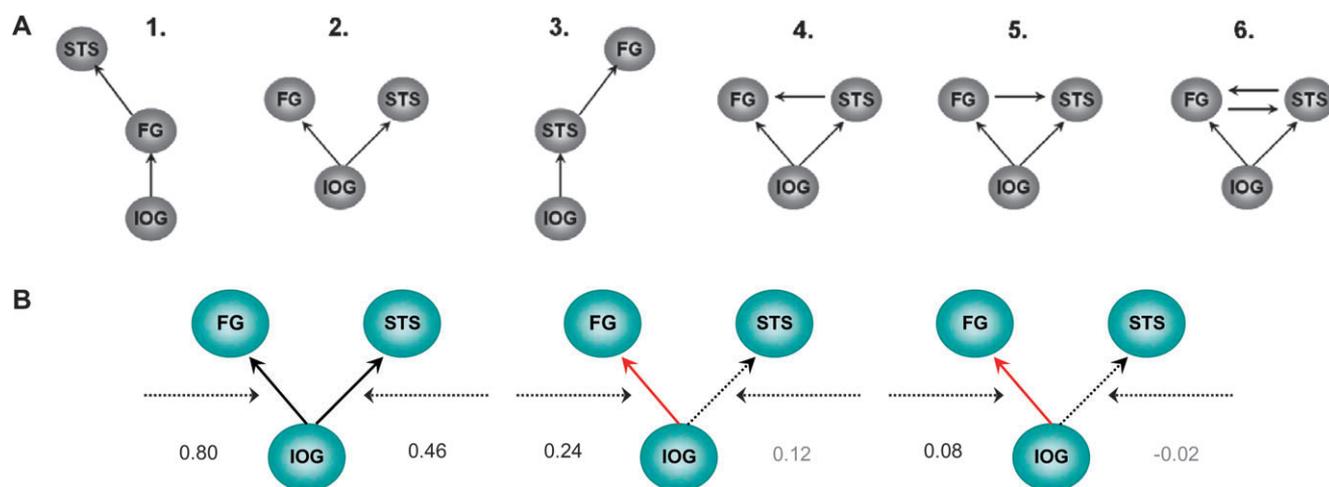
Figure 2. (A) Prototype models of the core system. Shown are the 6 feed-forward exemplars. Patterns of reciprocal connectivity were investigated by modifying the collateral and feedback connections. (B) Alterations in effective connectivity within the core system produced by all face stimuli, emotional faces, and famous faces. Black arrows indicate significant regional effects, red lines indicate significant bilinear effects, and dotted lines indicate nonsignificant effects.

effects are shown in Table 2. Faces per se had a strong and significant influence on the effective connectivity between the IOG and both the FG and STS (Fig. 2*B*). Although emotional and famous faces significantly increased the influence that the IOG exerted on the ventral (FG) pathway, this enabling effect was not observed along the dorsal (STS) pathway.

Effective Connectivity within the Left Hemisphere Core System

Functional brain imaging studies have consistently shown that the right hemisphere exhibits stronger response to face stimuli, in terms of both the number of subjects who show significant activation in face-responsive regions, and the spatial extent of the activation, that is, the cluster size (Sergent et al. 1992; Kanwisher et al. 1997; Haxby et al. 1999; Rossion et al. 2000; Ishai, Ungerleider, Martin, et al. 2000; Ishai et al. 2005; Kranz and Ishai 2006). To test whether the left hemisphere exhibits differential patterns of effective connectivity, we analyzed the regional and modulatory coupling in the 7 subjects who showed activation in the left IOG, FG, and STS (see Table 1). Consistent with the patterns of connectivity in the right hemisphere, we found greater evidence ($B = 2.9$) in favor of a direct and separate influence of the IOG on the FG and STS (Prototype 2, Fig. 2*A*) in 5 of 7 subjects. Moreover, we found that emotional and famous faces significantly increased the coupling between the IOG and the FG (Table 3).

The Extended System

Connectivity between the Core and the Extended Systems
To test our hypothesis that ventral rather than dorsal regions of the core system are functionally coupled with the extended system, the AMG, IFG, and OFC were connected in all varying combinations to either the FG or the STS in purely feed-forward

models (Supplementary Fig. 1). This analysis included the 5 subjects who showed activation in all regions of the extended system in the right hemisphere (see Table 1). Consistent with our hypothesis, model comparisons clearly favored a single FG connection to the extended system, with this model having much more evidence than the next best model ($B = 21.04$). Interestingly, the extent of evidence in favor of a model was seen to decrease on including the STS influence (Table 4).

Collateral and Feedback Connectivity
To assess the degree of lateral and reciprocal connections within the extended system, and the degree of feedback connectivity between the extended and core systems, a simplified set of models were constructed (Supplementary Fig. 1) and compared with a purely feed-forward model. Models which included lateral connections between regions of the extended system did not have greater evidence, nor did models that included both lateral and feedback connections (Table 5: bottom 2 rows). Bayesian selection could not distinguish between the purely feed-forward model and a model with backward regional connections from the extended to the core system (i.e., between A.1 and B.1 in Supplementary Fig. 1).

Functionally Selective Coupling within the Extended System
The more parsimonious feed-forward model (A.1 in Supplementary Fig. 1) was selected to investigate whether the effects of valence and fame can be expressed in terms of alterations in effective connectivity in the extended system (note that all patterns reported here were also present in the feedback model, see B.1 in Supplementary Fig. 1). In this model, valence and fame were allowed to influence all forward connections as bilinear terms. As in the core system, faces were observed to

Table 2

Effective connectivity within the right hemisphere core system

		Mean	SD	SEM	*P*
All faces	FG	0.80	0.21	0.07	0.0000
	STS	0.46	0.09	0.03	0.0000
Emotional faces	FG	0.24	0.17	0.05	0.0008
	STS	0.12	0.24	0.08	0.0796
Famous faces	FG	0.08	0.12	0.04	0.0265
	STS	−0.02	0.17	0.05	0.3819

Note: Means, standard deviations (SDs), standard error of the means (SEMs), and *P* values showing the alteration in effective connectivity within regions of the right hemisphere core system induced by all faces, emotional faces, and famous faces.

Table 3

Effective connectivity within the left hemisphere core system

		Mean	SD	SEM	*P*
All faces	FG	0.49	0.32	0.12	0.0064
	STS	0.27	0.27	0.10	0.0399
Emotional faces	FG	0.05	0.04	0.01	0.0130
	STS	0.08	0.12	0.05	0.1474
Famous faces	FG	0.11	0.09	0.04	0.0188
	STS	0.09	0.15	0.06	0.1737

Note: Means, standard deviations (SDs), standard error of the means (SEMs), and *P* values showing the alteration in effective connectivity within regions of the left hemisphere core system induced by all faces, emotional faces, and famous faces.

Table 4

Ventral and dorsal connections between the core and the extended systems

Model	Connections from the FG to:							
	AMG IFG OFC 1	IFG OFC 2	IFG AMG 3	OFC AMG 4	IFG 5	OFC 6	AMG 7	None 8
1		31.1	21.0	35.8	232.1	305.9	250.3	2693.6
2	0.0		0.7	1.2	7.5	9.9	8.1	86.7
3	0.0	1.5		1.7	11.0	14.5	11.9	128.0
4	0.0	0.9	0.6		6.5	8.5	7.0	75.2
5	0.0	0.1	0.1	0.2		1.3	1.1	11.6
6	0.0	0.1	0.1	0.1	0.8		0.8	8.8
7	0.0	0.1	0.1	0.1	0.9	1.2		10.8
8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	

Note: Each model in the rows is compared with each model in the columns. Models were arranged from high FG connectivity (left) to high STS connectivity (right). For clarity, only FG connections are indicated. The remaining region/s are connected to the STS.

Table 5

Patterns of reciprocal connectivity within the extended system

	Forward	Feedback	Collateral	Collateral and feedback
Forward only		1.2	14.8	4.4
Feedback connections	0.0		11.9	3.6
Collateral connectivity	0.0	0.0		0.3
Collateral and feedback	0.0	0.0	0.0	

Note: Each model (rows) was compared with the other models (columns). Models are depicted in Supplementary Figure 1.

increase the effective connectivity between the IOG and the FG and STS (Fig. 3). Faces were also observed to have a strong effect on the influence that the FG exerted on the AMG. Increases in effective connectivity between the FG, IFG, and OFC were apparent at a fixed effects level but were not significant across subjects (Table 6). Critically, valence and fame were observed to selectively enable dissociable pathways within the network for face perception: Viewing emotional faces produced an increase in effective connectivity along the IOG–FG–AMG pathway, whereas viewing famous faces increased coupling along the IOG–FG–OFC pathway (Fig. 3 and Table 6).

Discussion

In this study we employed conventional SPM with DCM to investigate the functional connections between regions of the cortical network that mediates face perception. This is, to our knowledge, the first use of Bayesian model selection to explore functional organization in a principled way. We found that in both hemispheres the core system is functionally organized in a hierarchical, feed-forward architecture, with the IOG exerting influences on both the FG and STS. Moreover, the FG, but not the STS, exerted a strong causal influence on the AMG, IFG, and OFC. Finally, within this network, we observed content-specific alterations in the functional coupling between visual-limbic regions and visual-prefrontal regions in response to emotional and famous faces, respectively.

Faces perception elicits activation within a distributed cortical network (Ishai et al. 2005) that includes all regions of the proposed core and extended systems (Haxby et al. 2000, 2002). Within the core system, the lateral FG plays a dominant role, as indicated by consistent and replicable patterns of activation within this region, irrespective of face formats, tasks, and experimental conditions (Kanwisher et al. 1997; Haxby et al. 1999; Ishai, Ungerleider, Haxby, 2000; Ishai, Ungerleider, Martin, et al. 2000; Grill-Spector et al. 2004; Kranz and Ishai 2006). Intriguingly, prosopagnosic patients, despite their profound inability to recognize faces, exhibit normal patterns of activation in the FG (Rossion et al. 2003; Avidan et al. 2005), suggesting that activation in the FG is insufficient for face recognition, which likely depends on integration across cortical regions. PS, a patient with bilateral and asymmetrical lesions, is prosopagnosic despite her intact left IOG and right FG, suggesting that activation in these 2 ventral regions of the core system in both hemispheres is necessary for face recognition (Rossion et al. 2003).

The STS, which mediates the processing of changeable aspects of faces (Hoffman and Haxby 2000; Haxby et al. 2002; Puce et al. 2003), is less reliably activated across subjects and tasks (e.g., Kanwisher et al. 1997; Haxby et al. 1999; Ishai et al. 2005). We therefore predicted that during attentive viewing the FG, and not the STS, would enable the dynamic coupling between visual and limbic/prefrontal face-selective regions. Our results indicate that the FG provides the major causal input into the extended system, which processes emotional and social aspects of face stimuli. Although the IOG was observed to separately and directly influence both the FG and the STS, the ventral and dorsal regions of the core system likely comprise 2 distinct pathways. As the FG exerted influences on all regions of the extended system (AMG, IFG, and OFC), it seems that the extraction of motile, changeable aspects of face stimuli within limbic and prefrontal regions are enabled via the ventral visual pathway.

It has been proposed that the STS plays a major role within a putative network for social cognition, which includes the AMG and the OFC (Brothers 1997; Allison et al. 2000; Adolphs 2003). According to this model, the STS, and not the FG, would exert the dominant influence on regions of the extended system implicated in social cognition. It should be noted that the static pictures used in our study provide an impoverished rendition of the social cues present in motile faces. During the perception of static faces, STS activation is thought to result from implied, rather than overt, biological motion (Haxby et al. 2002). We therefore predict that the STS would exert a greater effective influence on the extended system during the perception of animated faces. Future studies would determine whether such social cues are mediated through the FG, as suggested by our current study, or directly from the STS to the extended system.

When compared with neutral faces, emotional and famous faces elicit stronger activation within regions of the core and the extended systems (e.g., Vuilleumier et al. 2001; Pessoa et al. 2002; Ishai et al. 2004, 2005). It is believed that these manifestations of "valence enhancement" reflect top-down modulation or feedback processes. We hypothesized that attentive viewing of emotional faces would increase the effective connectivity between the FG and the AMG, which mediates the perception of emotional facial expressions, in particular fear, anger, and disgust (Breiter et al. 1996; Morris et al. 1996; Phillips et al. 1997; Ishai et al. 2004). Moreover, we predicted that viewing famous faces (taken from our database of contemporary Hollywood celebrities, see Ishai et al. 2002) would differentially increase the functional coupling between
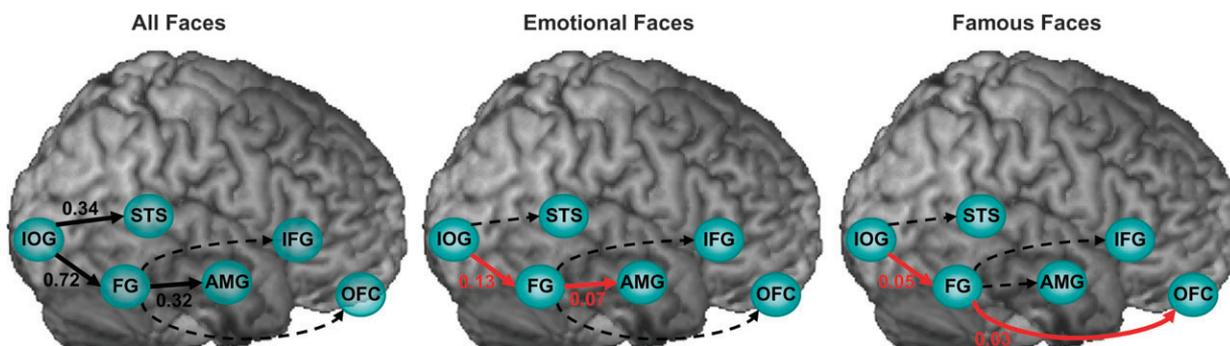
Figure 3. Alterations in effective connectivity within the core and the extended systems induced by all faces, emotional faces, and famous faces. Black connections indicate significant regional effects, red connections indicate significant bilinear effects, and dotted lines indicate nonsignificant effects.

Table 6
Content-specific coupling within the core and the extended systems

			Mean	SD	SEM	*P*
All faces	IOG	FG	0.72	0.17	0.08	0.0004
		STS	0.34	0.06	0.03	0.0001
	FG	IFG	0.14	0.37	0.16	0.2283
		OFC	0.17	0.28	0.12	0.1219
		AMG	0.32	0.08	0.03	0.0004
Emotional faces	IOG	FG	0.13	0.10	0.05	0.0232
		STS	0.08	0.12	0.06	0.1054
	FG	IFG	0.02	0.07	0.03	0.2786
		OFC	0.00	0.10	0.04	0.4605
		AMG	0.07	0.04	0.02	0.0144
Famous faces	IOG	FG	0.05	0.05	0.02	0.0314
		STS	0.01	0.07	0.03	0.4391
	FG	IFG	0.02	0.04	0.02	0.1154
		OFC	0.03	0.02	0.01	0.0171
		AMG	0.02	0.04	0.02	0.1866

Note: Across-subjects means, standard deviations (SDs), standard error of the means (SEMs), and *P* values indicate the alteration in effective connectivity induced by all faces, emotional, and famous faces within all regions.

the FG and the OFC, a region of the reward circuitry implicated in the processing of beautiful, attractive, and sexually relevant faces (O'Doherty et al. 2003; Kranz and Ishai 2006; Ishai 2007). Consistent with our hypothesis, the DCM analysis revealed content-specific alteration in effective connectivity between the core and the extended systems. Thus, emotional faces increased the effective connectivity between the IOG, FG, and the AMG, whereas famous faces increased the effective connectivity between the IOG, FG, and the OFC. These results demonstrate dynamic alterations in AMG and OFC activity, which depend on valence and fame-related aspects of face stimuli. Enhanced activation within the AMG and the OFC is caused (at least in part) by a differential increase in the influence that the FG exerts on these regions. Due to the large regional variability in hemodynamic response latencies, axonal conduction delays, which are typically in the order of 10–20 ms, cannot be estimated from fMRI data (Friston et al. 2003; Stephan et al. 2007). Future ERP or MEG studies will determine the temporal dynamics of coupling between these regions.

The Bayesian model selection consistently revealed greater evidence in favor of the simple, feed-forward models. The lack of evidence in favor of models with feedback and/or lateral connections does not reflect the absence of such anatomical connections, but rather, implies a unidirectional modulatory influence (see Friston et al. 2003; Penny et al. 2004a; Stephan et al. 2004). Thus, our results do not exclude the presence of reciprocal connections between regions of the extended system per se but suggest that these connections play a minor role in the observed hemodynamic response during face viewing. Our findings are also in accord with an intracranial recordings study, in which coupling (in the form of transient phase synchrony) between the FG and other cortical regions was observed during a delayed face recognition task, however, the other regions did not exhibit coupling with each other (Klopp et al. 2000).

We used attentive viewing to model the "default" network of face perception. Although face viewing elicits activation within multiple regions of the face network, not all subjects exhibit activation in all ROIs (e.g., Ishai et al. 2005). Previous studies have suggested that more engaging tasks are likely to evoke significant activation within all regions of the extended system (Ishai, Ungerleider, Martin, et al. 2000; Ishai et al. 2004; Kranz and Ishai 2006). The necessity to identify each and every region

in model construction renders DCM particularly susceptible to these variations in activation, with mandatory exclusion of subjects who did not show activation in all 6 ROIs of the face network. These differences in cortical activation likely reflect subject-specific variations in signal-to-noise ratio than variations in functional architecture. Future DCM studies may overcome these limitations by employing more cognitively demanding tasks that would enable the identification of all ROIs in all subjects.

In sum, our DCM analysis revealed that activation in limbic and prefrontal face-selective regions is modulated via the ventral visual stream, where the functional coupling between the FG and the AMG or the OFC is dynamically altered in response to distinct facial characteristics.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.

References

Adolphs R. 2003. Cognitive neuroscience of human social behaviour. Nat Rev Neurosci. 4:165–178.

Aharon I, Etcoff N, Ariely D, Chabris CF, O'Connor E, Breiter HC. 2001. Beautiful faces have variable reward value: fMRI and behavioral evidence. Neuron. 32:537–551.

Allison T, Puce A, McCarthy G. 2000. Social perception from visual cues: role of the STS region. Trends Cogn Sci. 4:267–278.

Avidan G, Hasson U, Malach R, Behrmann M. 2005. Detailed exploration of face-related processing in congenital prosopagnosia: 2. Functional neuroimaging findings. J Cogn Neurosci. 17:1150–1167.

Bitan T, Booth JR, Choy J, Burman DD, Gitelman DR, Mesulam MM. 2005. Shifts of effective connectivity within a language network during rhyming and spelling. J Neurosci. 25:5397–5403.

Breiter HC, Etcoff NL, Whalen PJ, Kennedy WA, Rauch SL, Buckner RL, Strauss MM, Hyman SE, Rosen BR. 1996. Response and habituation of the human amygdala during visual processing of facial expression. Neuron. 17:875–887.

Brothers L. 1997. Friday's footprint: how society shapes the human mind. New York: Oxford University Press.

Friston KJ, Harrison L, Penny W. 2003. Dynamic causal modelling. Neuroimage. 19:1273–1302.

Friston KJ, Holmes AP, Poline JB, Grasby PJ, Williams SC, Frackowiak RS, Turner R. 1995. Analysis of fMRI time-series revisited. Neuroimage. 2:45–53.

Friston KJ, Holmes AP, Worsley KJ, Poline J-P, Frith CD, Frackowiak RSJ. 1995. Statistical parametric maps in functional imaging: a general linear approach. Hum Brain Mapp. 2:189–210.

Grill-Spector K, Knouf N, Kanwisher N. 2004. The fusiform face area subserves face perception, not generic within-category identification. Nat Neurosci. 7:555–562.

Haxby JV, Hoffman EA, Gobbini MI. 2000. The distributed human neural system for face perception. Trends Cogn Sci. 4:223–233.

Haxby JV, Hoffman EA, Gobbini MI. 2002. Human neural systems for face recognition and social communication. Biol Psychiatry. 51:59–67.

Haxby JV, Ungerleider LG, Clark VP, Schouten JL, Hoffman EA, Martin A. 1999. The effect of face inversion on activity in human neural systems for face and object perception. Neuron. 22:189-199.

Haynes JD, Driver J, Rees G. 2005. Visibility reflects dynamic changes of effective connectivity between V1 and fusiform cortex. Neuron. 46:811-821.

Hoffman EA, Haxby JV. 2000. Distinct representations of eye gaze and identity in the distributed human neural system for face perception. Nat Neurosci. 3:80-84.

Ishai A. Forthcoming 2007. Sex, beauty and the orbitofrontal cortex. Int J Psychophysiol.

Ishai A, Haxby JV, Ungerleider LG. 2002. Visual imagery of famous faces: effects of memory and attention revealed by fMRI. Neuroimage. 17:1729-1741.

Ishai A, Pessoa L, Bikle PC, Ungerleider LG. 2004. Repetition suppression of faces is modulated by emotion. Proc Natl Acad Sci USA. 101:9827-9832.

Ishai A, Schmidt CF, Boesiger P. 2005. Face perception is mediated by a distributed cortical network. Brain Res Bull. 67:87-93.

Ishai A, Ungerleider LG, Haxby JV. 2000. Distributed neural systems for the generation of visual images. Neuron. 28:979-990.

Ishai A, Ungerleider LG, Martin A, Haxby JV. 2000. The representation of objects in the human occipital and temporal cortex. J Cogn Neurosci. 12:35-51.

Ishai A, Ungerleider LG, Martin A, Schouten JL, Haxby JV. 1999. Distributed representation of objects in the human ventral visual pathway. Proc Natl Acad Sci USA. 96:9379-9384.

Kanwisher N, McDermott J, Chun MM. 1997. The fusiform face area: a module in human extrastriate cortex specialized for face perception. J Neurosci. 17:4302-4311.

Kass RE, Raftery AE. 1993. Bayes factors and model uncertainty. Technical Report, University of Washington.

Klopp J, Marinkovic K, Chauvel P, Nenov V, Halgren E. 2000. Early widespread cortical distribution of coherent fusiform face selective activity. Hum Brain Mapp. 11:286-293.

Kranz F, Ishai A. 2006. Face perception is modulated by sexual preference. Curr Biol. 16:63-68.

Leveroni CL, Seidenberg M, Mayer AR, Mead LA, Binder JR, Rao SM. 2000. Neural systems underlying the recognition of familiar and newly learned faces. J Neurosci. 20:878-886.

Mechelli A, Price CJ, Friston KJ, Ishai A. 2004. Where bottom-up meets top-down: neuronal interactions during perception and imagery. Cereb Cortex. 14:1256-1265.

Mechelli A, Price CJ, Noppeney U, Friston KJ. 2003. A dynamic causal modeling study on category effects: bottom-up or top-down mediation? J Cogn Neurosci. 15:925-934.

Morris JS, Frith CD, Perrett DI, Rowland D, Young AW, Calder AJ, Dolan RJ. 1996. A differential neural response in the human amygdala to fearful and happy facial expressions. Nature. 383:812-815.

Noppeney U, Price CJ, Penny WD, Friston KJ. 2006. Two distinct neural mechanisms for category-selective responses. Cereb Cortex. 16:437-445.

O'Doherty J, Winston J, Critchley H, Perrett D, Burt DM, Dolan RJ. 2003. Beauty in a smile: the role of medial orbitofrontal cortex in facial attractiveness. Neuropsychologia. 41:147-155.

Penny WD, Stephan KE, Mechelli A, Friston KJ. 2004a. Modelling functional integration: a comparison of structural equation and dynamic causal models. Neuroimage. 23:264-274.

Penny WD, Stephan KE, Mechelli A, Friston KJ. 2004b. Comparing dynamic causal models. Neuroimage. 22:1157-1172.

Pessoa L, McKenna M, Gutierrez E, Ungerleider LG. 2002. Neural processing of emotional faces requires attention. Proc Natl Acad Sci USA. 99:11458-11463.

Phillips ML, Young AW, Senior C, Brammer M, Andrew C, Calder AJ, Bullmore ET, Perrett DI, Rowland D, Williams SC, et al. 1997. A specific neural substrate for perceiving facial expressions of disgust. Nature. 389:495-498.

Pruessmann KP, Weiger M, Scheidegger MB, Boesiger P. 1999. SENSE: sensitivity encoding for fast MRI. Magn Reson Med. 42:952-962.

Puce A, Syngeniotis A, Thompson JC, Abbott DF, Wheaton KJ, Castiello U. 2003. The human temporal lobe integrates facial form and motion: evidence from fMRI and ERP studies. Neuroimage. 19:861-869.

Rossion B, Caldara R, Seghier M, Schuller AM, Lazeyras F, Mayer E. 2003. A network of occipito-temporal face-sensitive areas besides the right middle fusiform gyrus is necessary for normal face processing. Brain. 126:2381-2395.

Rossion B, Dricot L, Devolder A, Bodart J-M, Crommelinck M, de Gelder B, Zoontjes R. 2000. Hemispheric asymmetries for whole-based and parts-based face processing in the human fusiform gyrus. J Cogn Neurosci. 12:793-802.

Sergent J, Ohta S, MacDonald B. 1992. Functional neuroanatomy of face and object processing. Brain. 115:15-36.

Smith AP, Stephan KE, Rugg MD, Dolan RJ. 2006. Task and content modulate amygdala-hippocampal connectivity in emotional retrieval. Neuron. 49:631-638.

Stephan KE, Harrison LM, Kiebel SJ, David O, Penny WD, Friston KJ. Forthcoming 2007. Dynamic causal models of neural system dynamics: current state and future extensions. J Biosci. 31.

Stephan KE, Harrison LM, Penny WD, Friston KJ. 2004. Biophysical models of fMRI responses. Curr Opin Neurobiol. 14:629-635.

Talairach J, Tournoux P. 1998. Co-planar stereotaxic atlas of the human brain. New York: Thieme Medical.

Vuilleumier P, Armony JL, Driver J, Dolan RJ. 2001. Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. Neuron. 30:829-841.