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Original Article

ORIGINAL ARTICLE

Frontoparietal Activity Interacts With Task-Evoked Changes in Functional Connectivity

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Abstract

Flexible interactions between brain regions enable neural systems to adaptively transfer and process information. However, the neural substrates that regulate adaptive communications between brain regions are understudied. In this human fMRI study, we investigated this issue by tracking time-varying, task-evoked changes in functional connectivity between localized occipitotemporal regions while participants performed different tasks on the same visually presented stimuli. We found that functional connectivity between ventral temporal and the primary visual regions selectively increased during the processing of task-relevant information. Further, additional task demands selectively strengthen these targeted connectivity patterns. To identify candidate regions that contribute to this increase in inter-regional coupling, we regressed the task-specific time-varying connectivity strength between primary visual and occipitotemporal regions against voxel-wise activity patterns elsewhere in the brain. This allowed us to identify a set of frontal and parietal regions whose activity increased as a function of task-evoked functional connectivity. These results suggest that frontoparietal regions may provide top-down biasing signals to influence task-specific interactions between brain regions.

Key words: cognitive control, frontal cortex, functional connectivity, parietal cortex

Introduction

The human brain is a complex system comprised of interconnected brain regions that are organized into distributed functional networks (Power et al. 2011; Yeo et al. 2011). This organizational structure offers a number of distinct information processing advantages. For instance, local neural responses can be transmitted across the network via structural connections, allowing the network to simultaneously support both local and integrated processes (Bullmore and Sporns 2012). These communication patterns are reflected in the dynamic activity among both local and distributed brain regions, which en masse define the spatiotemporal organization of brain activity (Honey et al. 2009). Past research suggests that these spatiotemporal patterns of brain activity can be adaptively modulated to enable flexible brain information processing, facilitating the execution of a range of complex behaviors (Shine and Poldrack 2017).

At the local level, neural responses within a functional brain region often exhibit task-dependent changes. For example, attending to sensory stimuli amplifies evoked-response amplitudes associated with the attended stimuli (Kastner et al. 1999; O'Craven et al. 1999; Druzgal and D'Esposito 2001), decreases evoked-response amplitudes associated with the distractor stimuli (Gazzaley et al. 2005), and sharpens tuning properties in cortical areas that represent the attended information (Fischer and Whitney 2009; Serences et al. 2009; Chen et al. 2012).

At the network level, inter-regional communication has been hypothesized to represent a key mechanism for brain information processing (Bullmore and Sporns 2009), and can be quantified by calculating the statistical dependency between activity in different brain regions (otherwise known as functional connectivity). Accordingly, it was proposed that information flow can

be selectively routed according to behavioral goals via feedback (or top-down) signals (Miller and Cohen 2001). In support of this hypothesis, attending to or memorizing visual stimuli has been shown to increase functional connectivity between early visual cortices that encode elementary visual features and higher level visual areas that represent more complex stimulus properties (Gazzaley et al. 2004; Al-Aidroos et al. 2012; Saalmann et al. 2012). Further, performing different behavioral tasks leads to different functional network configurations (Cole et al. 2014; Krienen et al. 2014; Mattar et al. 2015; Cohen and D'Esposito 2016), which likely reflect selective network reorganization in response to specific information processing demands.

The prefrontal cortex (PFC) and the posterior parietal cortex have been proposed to provide top-down biasing signals to influence sensory and motor processes (Miller and D'Esposito 2005; Cole et al. 2013). For example, attending to visual objects increases neural synchrony between lateral PFC and brain regions that represent the attended objects (Baldauf and Desimone 2014), whereas memorizing visual objects increases functional connectivity between frontoparietal regions and occipitotemporal brain regions that represent the to be memorized objects (Chadick and Gazzaley 2011; Kay and Yeatman 2017). Causal evidence indicates that increases in connectivity between the PFC and distributed brain regions likely reflect the PFC's role in exerting biasing signals to modulate evoked responses within local functional brain regions. For example, patients with PFC lesions showed increased distractor-related evoked responses in posterior cortices (Knight et al. 1999), and temporary disruption of PFC function with transcranial magnetic stimulation (TMS) in healthy individuals reduces stimulus-evoked responses amplitudes and decreases the discriminability of multivariate response patterns of activity within functional brain regions (Higo et al. 2011; Zanto et al. 2011; Lee and D'Esposito 2012).

In summary, the PFC and the parietal cortex can transmit top-down biasing signals to a targeted specific brain region and influence local evoked responses. In addition, functional connectivity between brain regions can be flexibly configured in response to specific information communication demands. Although several mechanisms have been proposed to explain top-down modulations of local evoked responses (Desimone and Duncan 1995; Cohen and Maunsell 2009; Serences et al. 2009), few studies have explored how biasing signals can adaptively modulate information flow along neural pathways at the network level. Previous studies have used structural equation modeling and dynamic causal modeling to model the contribution of feedforward inputs from early-level visual areas into higher-level areas along the visual pathways (e.g., middle temporal visual area and the posterior parietal cortex), and found that the posterior parietal cortex and the lateral PFC could enhance feedforward inputs to amplify responses in connected regions (Buchel and Friston 1997; Friston and Buchel 2000; Stephan et al. 2008). These studies however only test a limited number of cortical regions given the modeling constraint, and used a single stimulus category (motion dots).

The goal of our study was to use a factorial design in combination with whole-brain regression approach to comprehensively explore potential sources of top-down biasing signals that modulate task-evoked functional connectivity patterns. In this human fMRI study, we used a time-varying functional connectivity method (Shine et al. 2015) to estimate, with high temporal resolution, patterns of task-evoked functional interactions between primary and higher-level visual areas while subjects perform distinct tasks on the same categories of visual stimuli. Based on predictions from theoretical models as well as previous empirical observations, we hypothesized that different task demands can selectively modulate functional connectivity patterns between occipitotemporal areas to prioritize processing of task-relevant information. Further, by investigating the relationship between time-varying functional connectivity and whole brain activity, we were able to localize regions that may influence task-evoked functional connectivity patterns. Due to the correlational nature of our approach, we cannot conclude directionality, and any region we identified as putative sources of top-down biasing signals remain to be confirmed by future causal manipulation studies.

Methods

Subjects

In total, 29 healthy adults subjects were recruited for this study. Four subjects were excluded due to excessive head motion, thus, we report data from 25 subjects (aged 18–35, mean = 21.22, standard deviation [SD] = 2.44, 15 males). All subjects were right handed, had normal or corrected to normal vision and reported no history of a neurological or psychiatric disorder. All patients provided written informed consent in accordance with procedures approved by the Committee for the Protection of Human Subjects at the University of California, Berkeley.

Data Acquisition

Imaging data were acquired using a Siemens Tim/Trio 3 T scanner and a 12-channel head coil located at the Henry H. Wheeler Brain Imaging Center at University of California, Berkeley. Structural images were acquired using a multiecho MPRAGE sequence (TR = 2530 ms; TE = 1.64/3.5/5.36/7.22 ms; flip angle = 7°; field of view = 256 × 256, 176 sagittal slices, 1 mm^3 voxels; 2× GRAPPA acceleration). Functional images were acquired using an echo-planar sequence sensitive to blood oxygenated level-dependent (BOLD) contrast (TR = 1500 ms; TE = 25 ms; flip angel = 70°; field of view = 256 × 256, voxel size: 4 mm^3 isotropic voxels with 29 contiguous axial slices in descending order; no acceleration). Each subject completed 24 runs of functional scans, each run lasting 2 min and 33 s (102 volumes each, total = 2448 volumes; total scan time approximately 75 min). An LCD projector projected visual stimuli onto a screen mounted to the head coil. Psychophysics Toolbox Version 3 was used to present stimuli and record responses and via a fiber-optic motor response-recording device.

Experimental Tasks

In this fMRI experiment, subjects performed 2 different behavioral tasks on sequentially presented pictures randomly drawn from a set of 120 pictures of human faces and buildings. Specifically, each subject completed 8 runs of a functional localizer task, and 16 runs of experimental tasks (Fig. 1). The localizer task was used to independently identify regions of interests (ROIs) for the connectivity analyses. We used pictures of human faces for localizing the fusiform face area (FFA) (Kanwisher et al. 1997), pictures of buildings for the parahippocampal place area (PPA) (Epstein et al. 1999), and both categories for localizing the primary visual cortex (VC). For the primary experiment, we manipulated 2 experimental factors: task (categorization task vs. 1-back task) and the stimulus categories (faces vs. buildings). The same stimuli set was used for all tasks. In the localizer task and the categorization task, subjects were instructed to categorize pictures presented (a face or a building). For the 1-back task, subjects were instructed to detect occasional repetitions of one

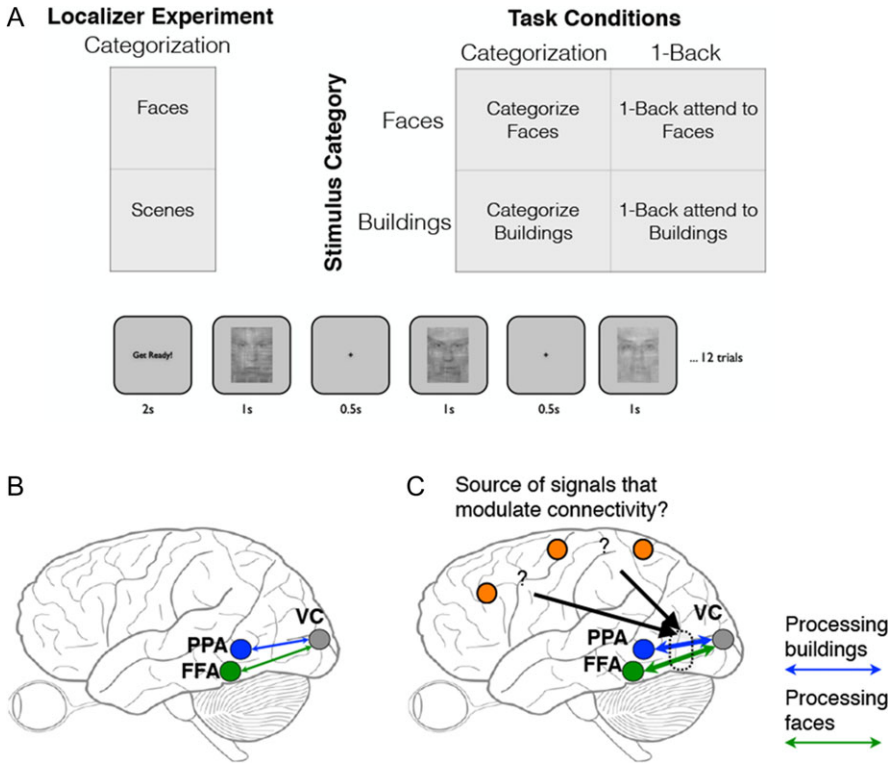

Figure 1. (*A*) Structure of the task and trial timing. (*B*) We hypothesized increased connectivity between VC and PPA when processing buildings, between VC and FFA when processing faces. (*C*) We hypothesized that patterns and strength of connectivity will be further modulated by task demands, and our goal was to localize potential sources that influence task-evoked functional connectivity.

stimulus category in the presence of competing stimuli from another category.

Each fMRI run contained only one task condition, and subjects were visually presented with detailed task instructions prior to the start of each run. All runs began with 3 s of initial fixation, followed by 4 task blocks (20 s each) interleaved with 3 baseline fixation blocks (20 s each), and a 10 s final fixation block (Fig. 1*A*). Each block started with a 2 s initiation cue. Task blocks consisted of 12 trials of stimuli. Each trial started with an image presented centrally on screen for 500 ms, immediately followed by a 1 s of fixation. For all tasks, subjects used their left or right index finger to respond. Specifically, in some runs subjects were asked to use their right index finger to respond to faces, left index finger for buildings, and vice versa for other runs. The response-mapping rules were randomized and balanced across tasks and runs.

For the localizer task, pictures of human faces or buildings were presented, and subjects were required to make a button press with the right or left index finger to identify the category of the picture presented (face or building). For the 1-back task, images presented were composited pictures of semitransparent faces overlapped with semitransparent buildings (Fig. 1). Prior to the start of each 1-back run, subjects were visually instructed to attend to a target category (faces or buildings), and detect the occasional back-to-back stimulus repetitions of the attended target category. Within each block, there were 2–4 repetitions for both stimulus categories, and the presentation sequences were randomized separately. Therefore, subjects were instructed to follow the response-mapping rule and make a button press only to the repeated stimuli of the attended category (2–4 responses per block), while ignoring luring repetitions from the potentially distractor category. For the categorization task, images were semitransparent faces or buildings overlaid on semitransparent phase-scrambled faces or buildings from the opposite category. The phase-scramble procedure ensured that elementary visual properties of stimuli used were equivalent between the 1-back and categorization tasks. There was no stimuli repetition in the categorize task, instead subjects were required to follow the response-mapping rule and make a button press with the right or left index finger to indicate the stimulus category of every presented picture (12 responses per block). Luminance for all pictures was equalized using the SHINE toolbox (Willenbockel et al. 2010). A feedback indicating the accuracy of responses from the previous run was given at the end of each run.

The functional and anatomical architecture of the visual system indicates that when perceiving visual objects, information related to elementary visual features encoded in primary VC is transmitted to anterior ventral temporal cortices that are sensitive to high-order, categorical information (Van Essen et al. 1992; Lerner et al. 2001; Kanwisher 2010). We hypothesized that the interaction between tasks (1-back vs. categorize) and stimuli categories (faces vs. buildings) would induce distinct task-evoked functional connectivity patterns among occipitotemporal brain regions. Based on results from previous studies (Gazzaley et al. 2004; Al-Aidroos et al. 2012), we hypothesized that the stimulus category will establish a specific functional interaction between the primary VC and the higher order visual areas more selective to a stimulus category (i.e., increased connectivity with FFA when processing faces vs. PPA when processing buildings; Fig. 1*B*). Different task conditions (1-back vs. categorize) will further modulate the strength of this functional connectivity. Both the categorization and the 1-back tasks require the primary VC to feedforward elementary visual features to higher-level visual areas (i.e., FFA/PPA) that

represent category-specific information. We hypothesized that the 1-back condition will induce additional feedback and feedforward interactions and further modify functional connectivity in a task-specific manner. Specifically, successfully performing the 1-back task requires memorizing visual features of the previously presented stimuli in absence of the external stimuli, and comparing the memorized features with those in the newly presented picture. This could be achieved by sustaining the interaction between elementary and category-specific visual information, and induce recurrent feedback and feedforward interactions between the primary VC and FFA/PPA. Additionally, because the categorize task utilized phase scrambled images for the stimuli from the opposite category, there is less competition between categories for identifying the stimulus identity. In contrast, the presence of competing distractors from an opposite stimulus category in the 1-back task will require biasing processes to enhance task-relevant information and inhibit task-irrelevant information, biasing processes that have been shown to not only modulate local brain activity (Gazzaley et al. 2005), but also strength of functional connectivity between occipitotemporal regions (Al-Aidroos et al. 2012). Our goal was to identify potential sources that modulate functional connectivity patterns according to different task demands (Fig. 1C).

Data Analysis

Preprocessing: Imaging data were processed using AFNI and FSL (Cox 1996; Smith et al. 2004). Functional images were slice-time and motion corrected (FSL's slicetimer and MC-FLIRT), coregistered to T1-weighted structural image using a boundary-based-registration algorithm (FSL's FLIRT), and warped to the MNI template using FSL's nonlinear registration (FSL's FNIRT). Functional data were then resampled to 2 mm combining motion correction and atlas transformation in a single interpolation step. Data were then spatially smoothed with a 5 mm full-width-at-half-maximum Gaussian kernel (FSL's SUSAN). We then performed nuisance regression using ordinary least squares regression (AFNI's 3dDeconvolve) with the following regressors: polynomial fits for removing linear drifts, 6 rigid-body motion parameters and its derivatives, averaged signal from white-matter and ventricles ROIs created using freesurfer's tissue segmentation tool (Dale et al. 1999). To minimize motion confounds, we calculated frame-wise displacement (FD) (Power et al. 2012), and volumes with FD > 0.2 were removed prior to all regression and MTD analyses to reduce variances associated with high noise timepoints (Power et al. 2013). No interpolation was performed. Subjects with > 25% volumes removed in any given run were also excluded (n = 4) because we wanted to preserve enough clean samples to properly estimate the coefficient for each regressor.

ROI analyses: After preprocessing, we performed a generalized linear model (GLM) analysis of linear regression at each voxel, using generalized least squares with a voxel-wise ARMA (1,1) autocorrelation model (AFNI's 3dREMLfit). Finite impulse response (FIR) basis functions were used to estimate the mean stimulus-evoked response amplitudes during task blocks, separately for each condition (localizers, categorize and 1-back conditions crossed with stimulus categories). Specifically, for every condition, a total of 20 FIR regressors were used to model 30 s of averaged block activities. Because each task block lasted 20 s, this model modeled 10 s out beyond the end of each task block to fully capture the rise and fall patterns of stimulus-evoked activities. Using data from the localizer runs, we then defined the FFA/PPA using the top 255 voxels (size equivalent to a sphere with 8 mm radius) that were most selective for faces (face blocks > building blocks) and buildings (building blocks > faces blocks) within previously defined FFA/PPA ROIs (Julian et al. 2012). We defined the early VC ROI using the top 255 most active voxels within an anatomically defined ROI of each individual subject's calcarine sulcus (Destrieux et al. 2010). To analyze differences in stimulus-evoked response amplitudes, for each ROI we performed a 3-way within subject analysis of variance, crossing conditions (1-back vs. categorize), stimulus categories (faces vs. buildings) and time (21 volumes within each task block).

Functional connectivity analyses: Our goal was to localize potential sources of top-down biasing signals that modulate task-evoked functional connectivity patterns. Achieving this goal requires a method that can estimate temporal changes in connectivity patterns under different task conditions, which can then be used in a regression model to localize regional changes in brain activity that covary with temporal changes in connectivity estimates. Thus, we utilized a time-varying functional connectivity metric, Multiplication of Temporal Derivatives (MTD) (for details see Shine et al. 2015), to estimate time varying connectivity strength between VC and PPA/FFA under task conditions. Prior to preforming all connectivity analyses, stimulus-evoked responses were regressed out from the preprocessed data, and residuals were used to assess task-evoked functional connectivity independent of shared variances between ROIs (Norman-Haignere et al. 2012; Cole et al. 2014; Gratton et al. 2016). This additional FIR regression was performed to minimize the influence of mean task-related stimulus-evoked activation on task-evoked functional connectivity, while retaining the residual trial-by-trial fluctuations in the time-series that contributes to task-evoked functional connectivity. A block design in combination with FIR modeling was chosen because block design summates stimulus-locked hemodynamic responses, which improves the power to detect stimulus-evoked activity (Bandettini and Cox 2000; Liu et al. 2001). Further, a data-driven FIR model does not assume the shape of stimulus-evoked responses, which is better at capturing different hemodynamic response profiles across brain regions. This mixed design reduces residual variance related to stimulus-induced evoked responses. We also modeled trail-level stimulus-evoked activity using 5 basis functions generated by FSL's linear optimal basis set (Woolrich et al. 2004), and results were comparable to those analyzed with FIR modeling. Across subjects, the mean correlation between residual timecourses from FIR and basis function models was 0.95 (SD = 0.08). Finally, for comparison we also performed time-varying functional connectivity analysis on data without FIR regression (Supplementary Fig. S1).

To perform MTD analysis, we first calculated the first order temporal derivatives (dt) of each time-series extracted from ROIs, and then normalized each data point by dividing each derivative by the SD of the whole time-series. We then multiplied dt scores to calculate MTD scores between ROIs. Positive MTD scores reflect synchronized coupling between ROIs, whereas negative MTD scores reflect out-of-synch decoupling. Similar to a Pearson correlation analysis, the MTD values can be averaged across time and be interpreted as static functional connectivity strength, whereas the time-varying MTD scores reflect dynamic changes in functional connectivity.

Because MTD scores of a single time point could be susceptible to high-frequency noise, we further calculated moving average on MTD scores using different moving average window lengths (Shine et al. 2015). To determine the most effective window length for detecting task-evoked functional connectivity

(i.e., connectivity between time-series that occurred primarily within task-blocks), we simulated time-series (Fig. 2A) that contained: (1) first order correlations over the entire task (task and resting blocks); and (2) second order correlations that occurred only during the task blocks (i.e., task correlations). We ran 5000 iterations of this simulation and calculated the MTD across a range of moving average window lengths from 10 to 100 volumes. We then determined the effect size of the difference between the task-evoked and resting correlation time-series (Fig. 2B). Moving average window with the length of 15 volumes showed the maximal effect size for differentiating first and second order functional connectivity. Therefore, all results were presented using a moving average window of 15 volumes, but we also explored a range of windows lengths (1–25). Importantly, MTD time-series for each condition can be used as additional regressors in the GLM analysis to localize potential sources of signals that modulate task-evoked functional connectivity patterns. We also performed seed-based connectivity analyses by including the mean signals extracted from FFA, PPA, VC as additional regressors along with all MTD regressors in the same GLM model.

Whole-brain GLM maps of each individual subject's MTD regressors were then submitted to group analysis contrasting the effects of condition (1-back vs. categorize) and its interaction with stimulus relevance (relevant stimuli, e.g., VC-FFA connectivity during attend to face condition, vs. irrelevant stimuli, e.g., VC-PPA connectivity during attend to face condition). Group level analysis was performed with a linear mixed effects model at each voxel, using generalized least squares with a local estimate of random effects variance (AFNI's 3dMEMA). To correct for multiple comparisons, we performed a nonparametric randomized permutation test to empirically derive the minimum cluster size that reached a corrected family-wise error rate of 0.05. Briefly, we randomly permuted the task condition (1-back vs. categorize) and recalculated the linear mixed effect model 1000 times. For each random permutation, we calculated the maximum cluster size that contained spatially contiguous voxels that exceeded the cluster forming threshold of $t(24) = 2.06$ ($P < 0.05$). We then pooled the results to derive an empirical null distribution of cluster sizes. This is the "null" distribution that satisfied the null hypothesis because task conditions were randomly assigned for each permutation, therefore, effects can only occur by chance. The value that was greater than 95% of values in the null distribution was used to determine the cluster size that reached a corrected family-wise error rate of 0.05. For all group analyses, we report corrected results using the cluster forming threshold of $t(24) = 2.06$ and corrected cluster size (corrected cluster size for MTD regressors were 688 contiguous 2 mm^3 voxels, for FFA/PPA seed regressors were 701 voxels, for VC seed regressors were 849 voxels). All unthresholded statistic maps have been uploaded to the NeuroVault database (http://neurovault.org/collections/2474/). The associated maps from seed-based regressors were submitted to group analysis using the same procedure.

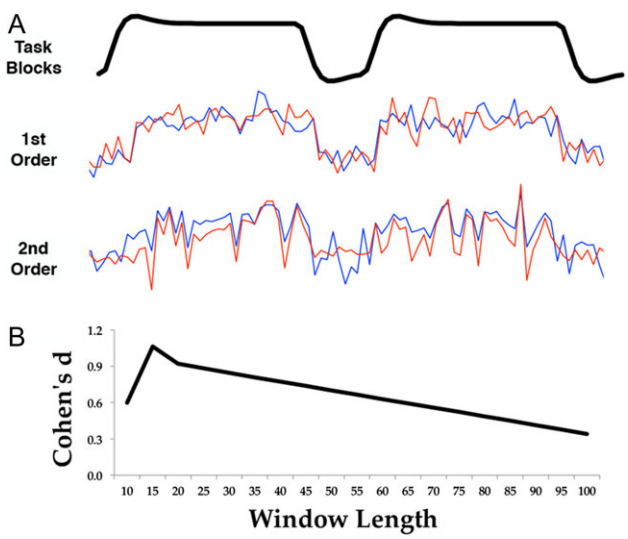

Figure 2. Simulation for determining optimal smoothing window. (A) Simulated time-series that have $r = 0.8$ correlations for both task and resting blocks (first order) or only during task blocks (second order). (B) Effect size of differentiating between first and second order correlations.

Connectivity and stimulus-evoked responses: We tested the relationship between MTD estimates and stimulus-evoked response amplitudes by calculating its correlations across subjects. The amplitudes of each condition's stimulus-evoked responses were calculated using area-under-the-curve of FIR estimates. We further correlated subject-by-subject seed-based connectivity strength estimates (Pearson correlations with FFA/PPA) from selected frontoparietal ROIs with stimulus-evoked response amplitudes. These ROIs were created by creating a 5 mm radius sphere centered on peak voxels in each significant spatial cluster that showed significant connectivity with FFA/PPA (right inferior precentral sulcus: $x = 20$, $y = -8$, $z = 56$; right insula: $x = 42$, $y = 24$, $z = 0$; right intraparietal sulcus: $x = 26$, $y = -58$, $z = 60$; left middle frontal: $x = 18$, $y = -36$, $z = 50$).

Results

Behavioral Results

Behavioral performance for the categorization task was near ceiling for both faces and buildings (mean accuracy for faces = 0.96, SD = 0.08; mean accuracy for buildings = 0.96, SD = 0.06; mean RT for faces = 543 ms, SD = 99 ms; mean RT for buildings = 557 ms, SD = 109 ms). Accuracy for detecting repetitions in the 1-back condition was below ceiling, and no significant difference was found between faces and buildings (mean accuracy for faces = 0.71, SD = 0.16; mean accuracy for buildings = 0.74, SD = 0.16; mean RT for faces = 745 ms, SD = 112 ms; mean RT for buildings = 693 ms, SD = 100 ms; t-test for accuracy: $t[24] = 1.07$, $P = 0.29$; t-test for RT: $t[24] = 7.39$, $P = 1.43 \times 10^{-7}$). The accuracy for 1-back (only including repeating stimuli) was significantly lower when compared with the categorize task (faces: $t[24] = 6.71$, $P = 7.27 \times 10^{-7}$; buildings: $t[24] = 1.02$, $P = 1.02 \times 10^{-7}$). Similarly, reaction time for 1-back task was significantly slower when compared with the categorization task (faces: $t[24] = 13.59$, $P = 7.17 \times 10^{-13}$; buildings: $t[24] = 8.39$, $P = 1.45 \times 10^{-8}$).

Stimulus Evoked Responses

We found increased stimulus-evoked responses in VC for all task conditions (Fig. 3A, main effect of factor volume: $F[1\ 2084] = 9.38$, $P = 0.0022$), but no significant condition by category interaction ($F[1\ 2084] = 0.31$, $P = 0.56$). We found significant condition by category interactions in both the FFA and PPA (Fig. 3B,C; FFA: $F[1\ 2084] = 4.21$, $P = 0.04$; PPA: $F[1\ 2084] = 4.87$, $P = 0.027$). Specifically, averaged across time points within task blocks, faces elicited stronger stimulus-evoked responses in FFA compared with buildings ($t[24] = 11.71$, $P = 1.82 \times 10^{-11}$), whereas buildings elicited a stronger responses in PPA compared with faces ($t(24) = 11.61$, $P = 2.18 \times 10^{-11}$). Further, for both the FFA and PPA, the 1-back condition elicited stronger stimulus-evoked

responses compared with the categorize condition (FFA: $t[24] = 4.29$, $P = 0.00032$; PPA: $t[24] = 5.39$, $P = 1.95 \times 10^{-5}$).

Time-Varying Functional Connectivity

Based on theoretical models and previous findings (Miller and Cohen, 2001; Al-Aidroos et al. 2012), we predicted that functional connectivity between VC and FFA/PPA should be modulated by stimulus category and task conditions. That is, when subjects attend to faces, functional connectivity between VC and FFA should increase compared with when they attended to buildings. In contrast, attention to buildings should increase connectivity between VC and PPA when compared with attention to faces. Further, when compared with the categorize task, the 1-back task should induce additional feedback and feedforward interactions between VC and FFA/PPA to maintain feature representations and compare with the newly presented stimulus, and to enhance task-relevant information in the presence of potentially distracting stimuli from the opposite stimulus category. Consistent with our predictions, we found that functional connectivity (calculated using time-averaged MTD scores) between task-related brain regions was modulated by both task and stimuli relevance (Fig. 4A). Specifically, functional connectivity between VC and PPA was stronger for the 1-back attend to buildings condition compared with the 1-back attend to faces condition ($t[24] = 6.51$, $P = 1.18 \times 10^{-6}$) and categorization conditions (1-back buildings vs. categorize faces: $t[24] = 5.98$, $P = 4.4 \times 10^{-6}$; 1-back buildings vs. categorize buildings: $t[24] = 3.27$, $P = 0.0032$). Functional connectivity between VC and FFA was significantly stronger for the 1-back attend to faces condition when compared with the 1-back attend to buildings condition ($t[24] = 4.44$, $P = 0.00017$) and categorize building condition (1-back faces vs. categorize faces: $t[24] = 1.98$, $P = 0.059$; 1-back faces vs. categorize buildings: $t[24] = 3.10$, $P = 0.003$). Connectivity between VC and FFA was stronger than VC and PPA under the 1-back attend to faces condition ($t[24] = 4.17$, $P = 0.00034$). No significant difference was found for connectivity between VC-PPA and VC-FFA under the 1-back attend to buildings condition ($t[24] = 0.17$, $P = 0.86$). These results were consistent across a range of smoothing windows we explored, ranging from 1TR to 25 TRs (Fig. 4B), and were further consistent with connectivity strength estimated using Pearson correlations (Fig. 4C). Furthermore, we did not find any significant correlations between evoked-response amplitudes and MTD estimates. MTD estimates for 1-back conditions were moderately correlated with subject's accuracy on the 1-back task (1-back attend to face: $r[24] = 0.37$, $P = 0.075$; 1-back attend to buildings $r(24) = 0.44$, $P = 0.031$).

Relationship Between Task-Evoked Time-Varying Functional Connectivity and Regional Activity

To localize potential sources of top-down biasing signals for modulating task-evoked functional connectivity, we entered each condition's time-varying MTD scores as additional regressors into a whole-brain GLM analysis and contrasted 1-back versus categorization conditions. We found that a distributed set of frontoparietal regions that showed increased activity that was positively associated with changes in task-evoked connectivity for processing task-relevant stimuli (i.e., averaging MTD estimates of VC-FFA for attend faces condition and VC-PPA for attend buildings conditions). These regions included bilateral superior frontal sulcus, the left middle frontal gyrus, bilateral dorsal medial frontal cortex, bilateral precuneus, and bilateral intraparietal sulcus (Fig. 5A). This indicates that increased activity in these frontal and parietal regions is associated with increases in connectivity strength between VC and higher order visual areas for processing the attended visual stimuli as a function of task-demands. No significant clusters of activation associated with processing of task-irrelevant stimuli were found after correcting form multiple comparisons.

Seed-Based Functional Connectivity

It is possible that the frontoparietal brain regions identified in the previous analysis were simultaneously interacting with

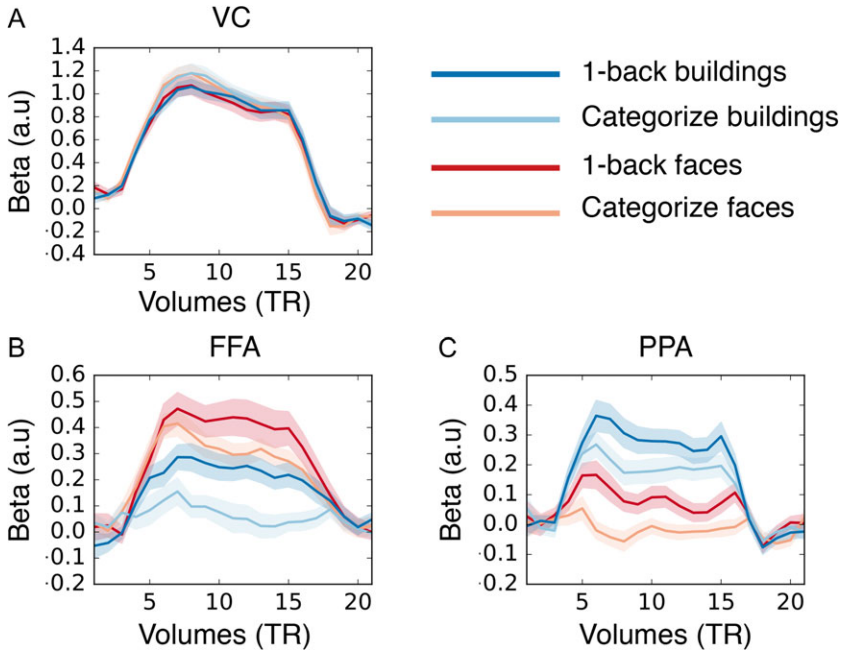

Figure 3. Stimulus-evoked responses. Y axis indicates stimulus-evoked response magnitude, X axis indicates the duration of task blocks. Shaded areas represent 1 SE (standard error).

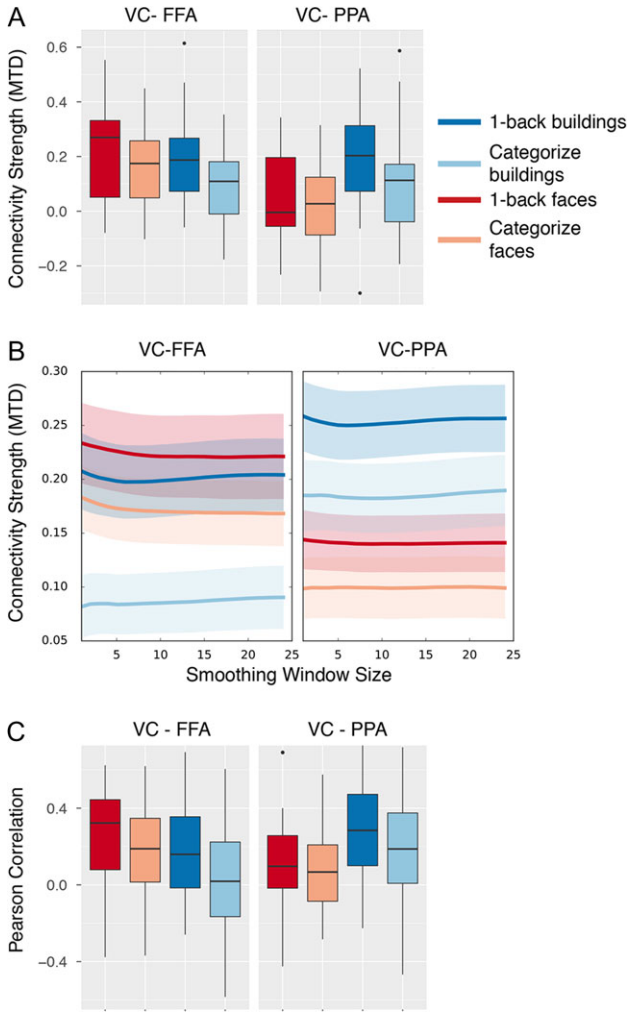

Figure 4. Task-evoked functional connectivity. (A) Box-plots of functional connectivity strength (MTD scores) between VC and FFA/PPA under different experimental conditions. Box plot percentiles (5th and 95th for outer whiskers, 25th and 75th for box edges, and median for horizontal line with the median) were calculated across subjects separately for each condition. Single dots represent values outside of 5th and 95th percentiles. (B) MTD scores across a range of smoothing window sizes. Thick solid lines represent the mean MTD values of each condition. Shaded areas represent 1 SE. (C) Box-plots of Pearson correlations calculated between VC and FFA for different conditions.

FFA/PPA and VC, but not specifically modulating functional connectivity strength between FFA/PPA and VC. To rule out this possibility, we performed additional seed-based functional connectivity analyses to localize brain regions that showed task-driven changes in connectivity (contrasting 1-back vs. categorize conditions) with FFA/PPA/VC. For functional connectivity analysis with FFA and PPA (Fig. 5B), we found increased connectivity with bilateral inferior precentral sulcus, the right inferior frontal gyrus, bilateral insular, the left intraparietal sulcus, bilateral occpitotemporal cortices, and the thalamus. We further found decreased connectivity with bilateral superior frontal sulcus, bilateral central sulcus, the dorsal medial PFC, bilateral inferior parietal cortex, bilateral medial occipital cortex, bilateral superior temporal cortex, and bilateral medial parietal cortex. For functional connectivity analysis with VC (Fig. 5C), we found increased connectivity with bilateral occipital, inferior temporal, posterior parietal, thalamus, and caudate. We further found decreased connectivity with bilateral central and precentral sulcus, superior temporal, superior frontal, insular, and medial parietal cortices. Importantly, except the intraparietal sulcus, most brain regions that showed increased functional connectivity with FFA/PPA/VC (Fig. 5B,C) exhibited little overlap with brain regions that showed a positive association with time-varying functional connectivity patterns (Fig. 5A). Instead, brain regions that showed decreased functional connectivity with FFA/PPA overlapped with brain regions that showed a positive association with time-varying functional connectivity patterns. No significant correlations were found between seed-based connectivity estimates and behavioral performance.

Control Analyses

To further investigate the effect of regressing out variance associated with stimulus-evoked responses, we repeated the time-varying functional connectivity analysis on data without FIR regression. We found that for both with and without FIR regression of stimulus-evoked responses, the results showed similar task by stimuli modulations of functional connectivity strength between VC and FFA/PPA. However, task differences were slightly weaker without FIR regression (Supplementary Fig. S1A). When comparing whole-brain regression map associated with task-evoked functional connectivity patterns, we found that both with and without FIR regression, results showed increased activity in the bilateral intraparietal sulcus and precuneus associated with task-evoked changes in functional connectivity between VC and FFA/PPA. In addition, analysis without FIR regression showed additional significant clusters in the left central and postcentral sulcus, and the right posterior temporal regions. Unlike our main analysis with FIR regression (Fig. 5A), data without FIR regression did not show increased activity in the PFC (Supplementary Fig. S1B).

Another potential concern is that the results presented in Figure 5A could be driven by covariations in residual stimulus-evoked activities that were not properly removed in our FIR regression. To demonstrate the specificity of our results, we selected 2 ROIs for further analysis (right inferior frontal: $x = -40$, $y = 26$, $z = 23$, right posterior parietal, anterior to the intraparietal cluster presented in Fig. 5A: $x = -29$, $y = -51$, $z = 49$). These 2 ROIs showed significant stimulus-evoked responses but did not showed increased activities in Figure 5A. We repeated the time-varying functional connectivity analysis, and regressed task-evoked functional connectivity patterns between those 2 ROIs against whole-brain activity (similar to those performed for Fig. 5A). This analysis yielded a distinct map (Supplementary Fig. S2), and only showed significant increases in the right insular, anterior frontal, and superior parietal cortices. This result suggests that regions presented in Figure 5A were specifically interacting with task-evoked functional connectivity patterns between VC and FFA/PPA, and not likely driven by covariations in residual stimulus-evoked activities.

Discussion

In this study, we investigated neural mechanisms underlying top-down biasing signals that modulate task-evoked, time-varying functional connectivity. In doing so, we found that task-related changes in functional connectivity patterns selectively interact with ongoing activity in a distributed system of frontal and parietal cortical regions. As such, our results suggest that these frontoparietal regions may be the source of

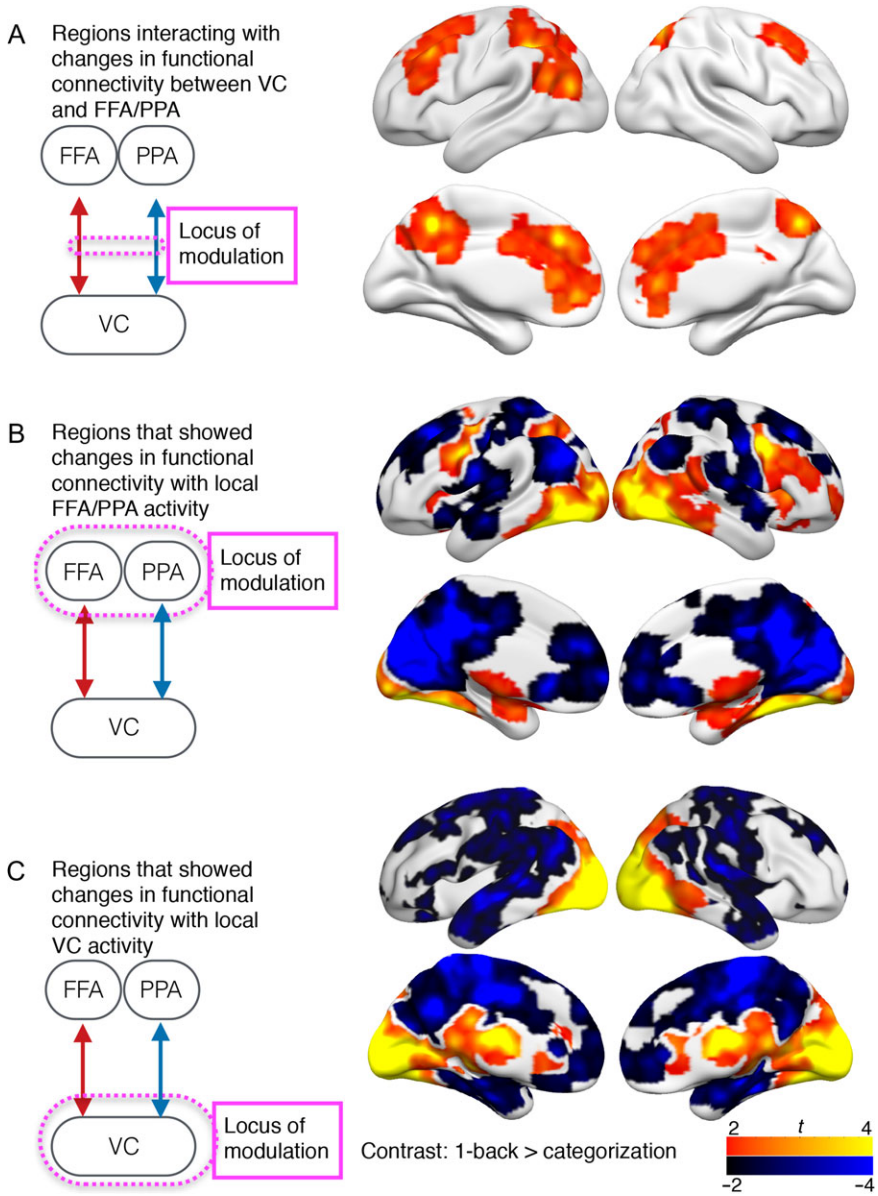

Figure 5. Potential sources of top-down biasing signals. (*A*) Regions that showed significant task modulations in interactions with task-evoked connectivity patterns between VC and FFA/PPA. This map was generated using a smoothing window of 15 volumes. (*B*) Regions that showed significant task-related changes in functional connectivity with local FFA/PPA activity. (*C*) Regions that showed significant task-related changes in functional connectivity with local VC activity. For all graphs, cluster forming threshold $P < 0.05$, corrected family-wise error rate = 0.05.

signals that bias information communication along functional pathways in response to task demands. This network level mechanism likely compliments other local mechanisms such as bias competition (Desimone and Duncan 1995), noise correlation (Cohen and Maunsell 2009), and tuning change (Serences et al. 2009), in support of flexible and adaptive behaviors.

Previous studies of patients with focal brain lesions or healthy individuals following TMS have provided ample evidence that frontal and parietal cortices provide top-down biasing signals that influence activity in posterior sensory cortices (Armstrong and Moore 2007; Ruff et al. 2008; Feredoes et al. 2011; Higo et al. 2011; Zanto et al. 2011; Lee and D'Esposito 2012; Gregoriou et al. 2014; Heinen et al. 2014; Lorenc et al. 2015). For example, TMS of dorsal lateral PFC (Feredoes et al. 2011), inferior frontal cortex (Zanto et al. 2011, Lee and D'Esposito 2012), frontal eye fields (Heinen et al. 2014), and intraparietal sulcus (Ruff et al. 2008) can modulate activity in occipitotemporal regions. In addition, stimulating the frontal cortex modulates the discriminability of the neural population code in occipitotemporal cortices (Armstrong and Moore 2007; Lee and D'Esposito 2012; Lorenc et al. 2015). Likewise, lateral PFC lesions reduce the attentional effect on stimulus-evoked response amplitudes and neural synchrony in V4 (Gregoriou et al. 2014). Studies have further demonstrated that frontal regions can selectively interact with specific brain regions in a task dependent manner (Gregoriou et al. 2009; Morishima et al. 2009; Baldauf and Desimone 2014). In aggregate, these studies suggest that one major function of frontoparietal cortices is to modulate the response amplitudes and tuning in functional brain regions. These empirical findings support the theory of

biased-competition (Desimone and Duncan 1995), which proposes that selection of goal-relevant information in specialized brain regions are enhanced by top-down biasing signals.

In addition to context-dependent changes in local brain responses, functional connectivity strength between task-related regions has also been shown to exhibit task-dependent changes (Gonzalez-Castillo et al. 2015; Gratton et al. 2016). The principal contribution of our study is to localize potential sources of biasing signals that modulate functional connectivity to several frontoparietal regions. These findings are further consistent with the proposed function of lateral PFC and posterior parietal cortex (Büchel et al. 1999; Friston and Buchel 2000; Miller and Cohen 2001). There are several potential mechanisms that could allow these regions to influence information flow among different brain regions. First, inter-regional communication has been proposed to be facilitated via temporal coherence of neural oscillations (Fries 2015). Therefore, one way to modulate inter-regional communication is to modulate the synchronization of neural oscillations between brain regions. It has been suggested that different classes of neural oscillations (i.e., alpha-, beta-, gamma-band oscillations) could be generated by distinct neurophysiological mechanisms (Moore et al. 2010; Wang 2010), and the expression of neural oscillations could be putatively controlled by neocortical inhibitory interneurons (Cardin et al. 2009; Vierling-Claassen et al. 2010). This suggests that top-down biasing signals emanating from frontoparietal cortices may influence cortical inhibitory neurons, modulate properties of neural oscillations, and in turn affect functional connectivity between brain regions.

A second potential mechanism could involve frontoparietal regions acting on the thalamus or the thalamic reticular nucleus (Wimmer et al. 2015), which in turn could modulate corticocortical communication. In addition to relaying information from peripheral sensory organs to the cerebral cortex, the thalamus has also been proposed to mediate the exchange of information between cortical regions through corticothalamic–cortical pathways (Sherman 2016). For example, the pulvinar nucleus synchronizes with distant cortical visual areas according to attentional demands (Saalmann et al. 2012). This suggests that the thalamus could receive top-down biasing signals from frontoparietal cortices, and in turn be involved in regulating information communication between cortical regions according in response to varying task demands. In our data, we did not observe thalamic activity that related to functional connectivity in visual regions, likely due to the reduced spatial resolution required by performing a whole brain analysis.

Another possibility is that changes in functional connectivity are down-stream effects induced by changes in local evoked-response amplitudes and tuning properties. For example, increased response amplitudes in one region could be the primary driver of activity in a connected region. In our analyses we removed the mean trial-evoked responses to alleviate the potential concern that our findings are driven by correlated increases in stimulus-evoked response amplitudes within the overlapped receptive fields between VC/FFA/PPA, but not changes in functional interactions. However, while FIR regression is effective in removing mean stimulus-evoked response that is common across all task blocks, there will still be stimulus-related activities that cannot be completely removed. Similarly, our regression approach cannot reveal nonlinear interactions between stimulus-driven and intrinsic brain activities. Thus, to further investigate the effect of stimulus-driven responses on our results, we conducted several control analyses. First, we correlated activity extracted from FFA/PPA/VC, and observed that the frontoparietal regions that exhibited increased static functional connectivity with FFA/PPA/VC (Fig. 5B,C) were different than the frontoparietal regions that correlated with time-varying functional connectivity patterns (Fig. 5A). Further, to demonstrate the specificity of the frontoparietal patterns we identified in Figure 5A were specifically covarying with task-evoked functional connectivity between visual regions, we repeated the same time-varying connectivity and regression analyses on 2 frontoparietal ROIs that exhibited task-positive responses. This analysis derived a distinct map (Supplementary Figure 2), which suggests that the frontoparietal activity we observed are likely not driven by residual stimulus-evoked responses that are common across all task-related ROIs. Finally, we found that estimates of time-varying functional connectivity strength did not correlate with evoked response amplitudes. Altogether, these results suggest the mechanisms that modulate task-evoked connectivity may be different from those that modulate localized evoked responses.

Since our results are correlative, we could not determine the direction of interaction between frontoparietal regions and task-evoked functional connectivity. It is possible that the frontoparietal activity we observed reflects a read out mechanism for selecting goal-relevant information, rather than a top-down biasing signal. Given previous findings demonstrating frontoparietal regions as the source of top-down biasing signals that modulate localized evoked responses, it is likely that frontoparietal regions also provide a biasing signal that can modulate task-evoked functional connectivity. TMS or lesion studies can directly test this prediction.

The frontoparietal regions we found to be correlated with changes in functional connectivity patterns also overlapped with brain regions previous reported as members of multiple intrinsic functional networks, such as the putative frontoparietal control network, the cingulo-opercular network, the dorsal attention network, and the default mode network (Greicius et al. 2003; Fox et al. 2006; Dosenbach et al. 2007; Seeley et al. 2007; Vincent et al. 2008). Each of these networks is proposed to subserve distinct cognitive functions. For example, the cingulo-opercular network is proposed to be involved in maintaining task-set information (Dosenbach et al. 2008), processing stimulus saliency (Seeley et al. 2007), or maintaining tonic alertness (Sadaghiani and D'Esposito 2015). In contrast, the frontoparietal network is proposed to be involved in trial-by-trial level adaptive control, such as performance feedback (Dosenbach et al. 2008), whereas the dorsal attention network is proposed to be involved in directing attention to select goal-relevant stimuli (Corbetta and Shulman 2002). Finally, the default mode network is proposed to integrate information across perceptual and motor systems in memory tasks (Vatansever et al. 2015). It is likely that our task engages both sustained and transient control processes that have been associated with these networks, and these control processes will in turn influence information transfer between brain regions. Causal TMS or lesion studies can determine if the different frontoparietal regions we found exert distinct top-down biasing signals to differentially modulate functional interactions under different contexts.

Supplementary Material

Supplementary material is available at *Cerebral Cortex* online.

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References

Al-Aidroos N, Said CP, Turk-Browne NB. 2012. Top-down attention switches coupling between low-level and high-level areas of human visual cortex. Proc Natl Acad Sci USA. 109: 14675–14680.

Armstrong KM, Moore T. 2007. Rapid enhancement of visual cortical response discriminability by microstimulation of the frontal eye field. Proc Natl Acad Sci USA. 104: 9499–9504.

Baldauf D, Desimone R. 2014. Neural mechanisms of object-based attention. Science. 344:424–427.

Bandettini PA, Cox RW. 2000. Event-related fmri contrast when using constant interstimulus interval: theory and experiment. Magn Reson Med. 43:540–548.

Büchel C, Coull JT, Friston KJ. 1999. The predictive value of changes in effective connectivity for human learning. Science. 283:1538–1541.

Buchel C, Friston KJ. 1997. Modulation of connectivity in visual pathways by attention: cortical interactions evaluated with structural equation modelling and fMRI. Cereb Cortex. 7: 768–778.

Bullmore E, Sporns O. 2009. Complex brain networks: graph theoretical analysis of structural and functional systems. Nat Rev Neurosci. 10:186–198.

Bullmore E, Sporns O. 2012. The economy of brain network organization. Nat Rev Neurosci. 13:336–349.

Cardin J, Carlén M, Meletis K, Knoblich U, Zhang F, Deisseroth K, Tsai L, Moore C. 2009. Driving fast-spiking cells induces gamma rhythm and controls sensory responses. Nature. 459 (7247):663–667.

Chadick JZ, Gazzaley A. 2011. Differential coupling of visual cortex with default or frontal-parietal network based on goals. Nat Neurosci. 14:830–832.

Chen AJ, Britton M, Turner GR, Vytlacil J, Thompson TW, D'Esposito M. 2012. Goal-directed attention alters the tuning of object-based representations in extrastriate cortex. Front Hum Neurosci. 6:187.

Cohen JR, D'Esposito M. 2016. The segregation and integration of distinct brain networks and their relationship to cognition. J Neurosci. 36:12083–12094.

Cohen MR, Maunsell JH. 2009. Attention improves performance primarily by reducing interneuronal correlations. Nat Neurosci. 12:1594–1600.

Cole MW, Bassett DS, Power JD, Braver TS, Petersen SE. 2014. Intrinsic and task-evoked network architectures of the human brain. Neuron. 83:238–251.

Cole MW, Reynolds JR, Power JD, Repovs G, Anticevic A, Braver TS. 2013. Multi-task connectivity reveals flexible hubs for adaptive task control. Nat Neurosci. 16:1348–1355.

Corbetta M, Shulman G. 2002. Control of goal-dircted and stimulus-drive attention in the brain. Nat Rev Neurosci. 3: 215–229.

Cox RW. 1996. Afni: software for analysis and visualization of functional magnetic resonance neuroimages. Comput Biomed Res. 29:162–173.

Dale AM, Fischl B, Sereno MI. 1999. Cortical surface-based analysis. I. Segmentation and surface reconstruction. NeuroImage. 9:179–194.

Desimone R, Duncan J. 1995. Neural mechanisms of selective visual attention. Annu Rev Neurosci. 18:193–222.

Destrieux C, Fischl B, Dale A, Halgren E. 2010. Automatic parcellation of human cortical gyri and sulci using standard anatomical nomenclature. NeuroImage. 53:1–15.

Dosenbach NU, Fair DA, Cohen AL, Schlaggar BL, Petersen SE. 2008. A dual-networks architecture of top-down control. Trends Cogn Sci. 12:99–105.

Dosenbach NU, Fair DA, Miezin FM, Cohen AL, Wenger KK, Dosenbach RA, Fox MD, Snyder AZ, Vincent JL, Raichle ME, et al. 2007. Distinct brain networks for adaptive and stable task control in humans. Proc Natl Acad Sci USA. 104: 11073–11078.

Druzgal TJ, D'Esposito M. 2001. Activity in fusiform face area modulated as a function of working memory load. Brain Res Cogn Brain Res. 10:355–364.

Epstein R, Harris A, Stanley D, Kanwisher N. 1999. The parahippocampal place area: recognition, navigation, or encoding? Neuron. 23:115–125.

Feredoes E, Heinen K, Weiskopf N, Ruff C, Driver J. 2011. Causal evidence for frontal involvement in memory target maintenance by posterior brain areas during distracter interference of visual working memory. Proc Natl Acad Sci USA. 108: 17510–17515.

Fischer J, Whitney D. 2009. Attention narrows position tuning of population responses in V1. Curr Biol. 19:1356–1361.

Fox MD, Corbetta M, Snyder AZ, Vincent JL, Raichle ME. 2006. Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. Proc Natl Acad Sci USA. 103: 10046–10051.

Fries P. 2015. Rhythms for cognition: communication through coherence. Neuron. 88:220–235.

Friston KJ, Buchel C. 2000. Attentional modulation of effective connectivity from V2 to V5/MT in humans. Proc Natl Acad Sci USA. 97:7591–7596.

Gazzaley A, Cooney JW, McEvoy K, Knight RT, D'Esposito M. 2005. Top-down enhancement and suppression of the magnitude and speed of neural activity. J Cogn Neurosci. 17: 507–517.

Gazzaley A, Rissman J, D'Esposito M. 2004. Functional connectivity during working memory maintenance. Cogn Affect Behav Neurosci. 4:580.

Gonzalez-Castillo J, Hoy CW, Handwerker DA, Robinson ME, Buchanan LC, Saad ZS, Bandettini PA. 2015. Tracking ongoing cognition in individuals using brief, whole-brain functional connectivity patterns. Proc Natl Acad Sci USA. 112: 8762–8767.

Gratton C, Laumann TO, Gordon EM, Adeyemo B, Petersen SE. 2016. Evidence for two independent factors that modify brain networks to meet task goals. Cell Rep. 17: 1276–1288.

Gregoriou GG, Gotts SJ, Zhou H, Desimone R. 2009. High-frequency, long-range coupling between prefrontal and visual cortex during attention. Science. 324:1207–1210.

Gregoriou GG, Rossi AF, Ungerleider LG, Desimone R. 2014. Lesions of prefrontal cortex reduce attentional modulation of neuronal responses and synchrony in V4. Nat Neurosci. 17:1003–1011.

Greicius MD, Krasnow B, Reiss AL, Menon V. 2003. Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. Proc Natl Acad USA. 100:253–258.

Heinen K, Feredoes E, Weiskopf N, Ruff CC, Driver J. 2014. Direct evidence for attention-dependent influences of the frontal eye-fields on feature-responsive visual cortex. Cereb Cortex. 24:2815–2821.

Higo T, Mars RB, Boorman ED, Buch ER, Rushworth MF. 2011. Distributed and causal influence of frontal operculum in task control. Proc Natl Acad Sci USA. 108:4230–4235.

Honey CJ, Sporns O, Cammoun L, Gigandet X, Thiran JP, Meuli R, Hagmann P. 2009. Predicting human resting-state functional connectivity from structural connectivity. Proc Natl Acad Sci USA. 106:2035–2040.

Julian JB, Fedorenko E, Webster J, Kanwisher N. 2012. An algorithmic method for functionally defining regions of interest in the ventral visual pathway. Neuroimage. 60: 2357–2364.

Kanwisher N. 2010. Functional specificity in the human brain: a window into the functional architecture of the mind. Proc Natl Acad Sci USA. 107:11163–11170.

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.

Kastner S, Pinsk MA, De Weerd P, Desimone R, Ungerleider LG. 1999. Increased activity in human visual cortex during directed attention in the absence of visual stimulation. Neuron. 22:751–761.

Kay KN, Yeatman JD. 2017. Bottom-up and top-down computations in word- and face-selective cortex. eLife. 6:e22341. doi:10.7554/eLife.22341.

Knight RT, Staines WR, Swick D, Chao LL. 1999. Prefrontal cortex regulates inhibition and excitation in distributed neural networks. Acta Psychol (Amst). 101:159–178.

Krienen FM, Yeo BT, Buckner RL. 2014. Reconfigurable task-dependent functional coupling modes cluster around a core functional architecture. Philos Trans R Soc Lond B Biol Sci. 369. doi:10.1098/rstb.2013.0526.

Lee TG, D'Esposito M. 2012. The dynamic nature of top-down signals originating from prefrontal cortex: a combined fMRI-TMS study. J Neurosci. 32:15458–15466.

Lerner Y, Hendler T, Ben-Bashat D, Harel M, Malach R. 2001. A hierarchical axis of object processing stages in the human visual cortex. Cereb Cortex. 11:287–297.

Liu TT, Frank LR, Wong EC, Buxton RB. 2001. Detection power, estimation efficiency, and predictability in event-related fMRI. NeuroImage. 13:759–773.

Lorenc ES, Lee TG, Chen AJ, D'Esposito M. 2015. The effect of disruption of prefrontal cortical function with transcranial magnetic stimulation on visual working memory. Front syst Neurosci. 9:169.

Mattar MG, Cole MW, Thompson-Schill SL, Bassett DS. 2015. A functional cartography of cognitive systems. PLoS Comput Biol. 11:e1004533.

Miller EK, Cohen JD. 2001. An integrative theory of prefrontal cortex function. Annu Rev Neurosci. 24:167–202.

Miller BT, D'Esposito M. 2005. Searching for "the top" in top-down control. Neuron. 48:535–538.

Moore CI, Carlen M, Knoblich U, Cardin JA. 2010. Neocortical interneurons: from diversity, strength. Cell. 142:189–193.

Morishima Y, Akaishi R, Yamada Y, Okuda J, Toma K, Sakai K. 2009. Task-specific signal transmission from prefrontal cortex in visual selective attention. Nat Neurosci. 12:85–91.

Norman-Haignere SV, McCarthy G, Chun MM, Turk-Browne NB. 2012. Category-selective background connectivity in ventral visual cortex. Cereb Cortex. 22:391–402.

O'Craven KM, Downing PE, Kanwisher N. 1999. Fmri evidence for objects as the units of attentional selection. Nature. 401: 584–587.

Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE. 2012. Spurious but systematic correlations in functional connectivity mri networks arise from subject motion. NeuroImage. 59:2142–2154.

Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE. 2013. Steps toward optimizing motion artifact removal in functional connectivity MRI; a reply to Carp. Neuroimage. 76:439–441.

Power JD, Cohen AL, Nelson SM, Wig GS, Barnes KA, Church JA, Vogel AC, Laumann TO, Miezin FM, Schlaggar BL, et al. 2011. Functional network organization of the human brain. Neuron. 72:665–678.

Ruff CC, Bestmann S, Blankenburg F, Bjoertomt O, Josephs O, Weiskopf N, Deichmann R, Driver J. 2008. Distinct causal influences of parietal versus frontal areas on human visual cortex: evidence from concurrent TMS-fMRI. Cereb Cortex. 18:817–827.

Saalmann YB, Pinsk MA, Wang L, Li X, Kastner S. 2012. The pulvinar regulates information transmission between cortical areas based on attention demands. Science. 337:753–756.

Sadaghiani S, D'Esposito M. 2015. Functional characterization of the cingulo-opercular network in the maintenance of tonic alertness. Cereb Cortex. 25:2763–2773.

Seeley WW, Menon V, Schatzberg AF, Keller J, Glover GH, Kenna H, Reiss AL, Greicius MD. 2007. Dissociable intrinsic connectivity networks for salience processing and executive control. J Neurosci. 27:2349–2356.

Serences JT, Saproo S, Scolari M, Ho T, Muftuler LT. 2009. Estimating the influence of attention on population codes in human visual cortex using voxel-based tuning functions. Neuroimage. 44:223–231.

Sherman SM. 2016. Thalamus plays a central role in ongoing cortical functioning. Nat Neurosci. 16:533–541.

Shine JM, Koyejo O, Bell PT, Gorgolewski KJ, Gilat M, Poldrack RA. 2015. Estimation of dynamic functional connectivity using Multiplication of Temporal Derivatives. Neuroimage. 122:399–407.

Shine JM, Poldrack RA 2017. Principles of dynamic network reconfiguration across diverse brain states. Neuroimage.

Smith SM, Jenkinson M, Woolrich MW, Beckmann CF, Behrens TE, Johansen-Berg H, Bannister PR, De Luca M, Drobnjak I, Flitney DE, et al. 2004. Advances in functional and structural mr image analysis and implementation as fsl. NeuroImage. 23(Suppl 1):S208–S219.

Stephan KE, Kasper L, Harrison LM, Daunizeau J, den Ouden HE, Breakspear M, Friston KJ. 2008. Nonlinear dynamic causal models for fMRI. Neuroimage. 42:649–662.

Van Essen DC, Anderson CH, Felleman DJ. 1992. Information processing in the primate visual system: an integrated systems perspective. Science. 255:419–422.

Vatansever D, Menon DK, Manktelow AE, Sahakian BJ, Stamatakis EA. 2015. Default mode dynamics for global functional integration. J Neurosci. 35:15254–15262.

Vierling-Claassen D, Cardin JA, Moore CI, Jones SR. 2010. Computational modeling of distinct neocortical oscillations driven by cell-type selective optogenetic drive: separable resonant circuits controlled by low-threshold spiking and fast-spiking interneurons. Front Hum Neurosci. 4:198.

Vincent JL, Kahn I, Snyder AZ, Raichle ME, Buckner RL. 2008. Evidence for a frontoparietal control system revealed by

intrinsic functional connectivity. J Neurophysiol. 100(6): 3328–3342.

Wang X-J. 2010. Neurophysiological and computational principles of cortical rhythms in cognition. Physiol Rev. 90: 1195–1268.

Willenbockel V, Sadr J, Fiset D, Horne GO, Gosselin F, Tanaka JW. 2010. Controlling low-level image properties: the SHINE toolbox. Behav Res Methods. 42:671–684.

Wimmer RD, Schmitt LI, Davidson TJ, Nakajima M, Deisseroth K, Halassa MM. 2015. Thalamic control of sensory selection in divided attention. Nature. 526:705–709.

Woolrich MW, Behrens TEJ, Smith SM. 2004. Constrained linear basis sets for HRF modelling using Variational Bayes. Neuroimage. 21:1748–1761.

Yeo BT, Krienen FM, Sepulcre J, Sabuncu MR, Lashkari D, Hollinshead M, Roffman JL, Smoller JW, Zollei L, Polimeni JR, et al. 2011. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol. 106:1125–1165.

Zanto TP, Rubens MT, Thangavel A, Gazzaley A. 2011. Causal role of the prefrontal cortex in top-down modulation of visual processing and working memory. Nat Neurosci. 14:656–661.