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Differential coupling of visual cortex with default or frontal-parietal network based on goals

James Z Chadick & Adam Gazzaley

The relationship between top-down enhancement and suppression of sensory cortical activity and large-scale neural networks remains unclear. Functional connectivity analysis of human functional magnetic resonance imaging data revealed that visual cortical areas that selectively process relevant information are functionally connected with the frontal-parietal network, whereas those that process irrelevant information are simultaneously coupled with the default network. This indicates that sensory cortical regions are differentially and dynamically coupled with distinct networks on the basis of task goals.

Goal-directed decisions influence our perception and result in corresponding modulation of sensory cortical activity. This phenomenon, known as top-down modulation, is characterized by increased cortical responses when stimuli are task-relevant (enhancement) and decreased responses when stimuli are task-irrelevant (suppression)[1,2]. It is this modulatory ability that allows us to successfully navigate multiple streams of sensory information in a flexible manner. Top-down modulation is not thought to be an intrinsic property of visual cortices, but is instead achieved via distributed connections between brain regions or neural networks, notably involving the prefrontal cortex, parietal cortex and the visual association cortex[3–5]. Recent evidence suggests that enhancement and suppression are distinct neural processes; for example, they are differentially affected by aging[6] and cognitive load manipulations[7].

Similar to top-down modulation of sensory cortices, distinct sets of parietal and frontal regions exhibit enhanced and suppressed activity depending on an individual's goals. Specifically, the frontal-parietal network (FPN)[8,9] is co-activated during a wide array of externally directed tasks (for example, selective attention[3,10]), whereas the default network[9,11] is de-activated during these tasks[11] and activated by introspective cognitive processes (for example, prospective/retrospective memory and internal monitoring[12]). To the best of our knowledge, the relationship between these large-scale networks and top-down enhancement and suppression of sensory cortical activity has not been reported.

We evaluated whole-brain networks associated with top-down modulation in the setting of simultaneous, competing visual processing demands. We used functional magnetic resonance imaging (fMRI) during a selective, delayed-recognition task in which participants were required to remember specific stimuli while simultaneously ignoring irrelevant stimuli (superimposed faces and natural scenes) over a brief delay period[13] (**Fig. 1**). Both working memory accuracy and response time were negatively affected by the presence of irrelevant stimuli, compared to trials where relevant stimuli were presented in isolation (**Supplementary Results** and **Supplementary Fig. 1**). To derive measures of neural enhancement and suppression, we assessed encode period activity in scene-selective visual association cortex (parahippocampal place area, PPA) and face-selective regions (fusiform face area, FFA)[1,3,7]. We found significant top-down modulation in the PPA, such that there was enhancement of activity when scenes were relevant compared with passive-view baseline (scene-memory overlap (SM-O) > passive-view overlap (PV-O), $P < 0.001$) and suppression when scenes were irrelevant (PV-O > face-memory overlap (FM-O), $P < 0.005$) (**Supplementary Fig. 2a**), consistent with previous findings using sequentially presented images[1]. This activity modulation represents a pure top-down effect, as bottom-up (stimulus-driven)

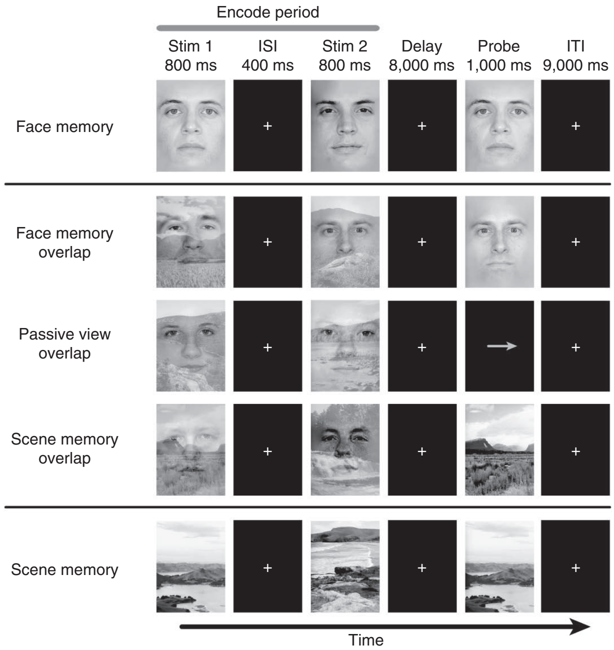

Figure 1 Experimental procedure. Participants were instructed to remember stimulus 1 (stim 1) and stimulus 2 (stim 2) and respond with either yes or no if the probe image matched either of the previous two relevant stimuli, as indicated by the task instructions. Participants maintained fixation on the white crosshairs throughout experiment. ISI, inter-stimulus interval; ITI, inter-trial interval. All participants provided informed, written consent in accordance with the Committee on Human Research oversight board at the University of California, San Francisco.

Department of Neurology, Physiology and Psychiatry, W.M. Keck Foundation Center for Integrative Neuroscience, University of California, San Francisco, USA. Correspondence should be addressed to A.G. (adam.gazzaley@ucsf.edu).

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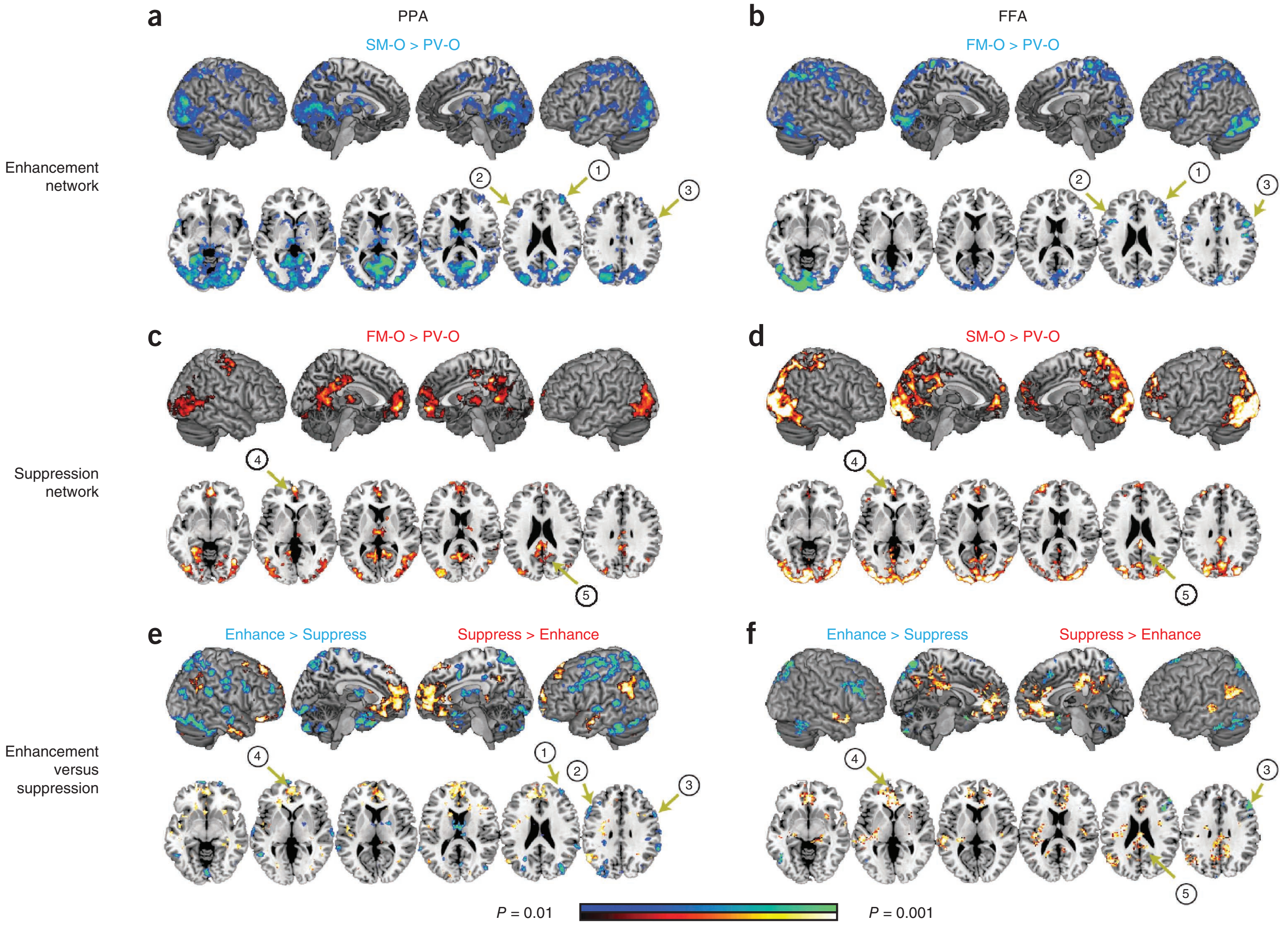

Figure 2 Network connectivity. (**a**–**f**) Connectivity maps associated with enhancement (SM-O > PV-O, **a**; FM-O > PV-O, **b**) and suppression (FM-O > PV-O, **c**; SM-O > PV-O, **d**) and contrast maps between suppression and enhancement networks (**e**,**f**) for both PPA (**a**,**c**,**e**) and FFA (**b**,**d**,**f**). Whole-brain maps were cluster-corrected for multiple comparisons at $P = 0.05$ and displayed at $P < 0.01$. Labeled regions are as follows: 1, right middle frontal gyrus; 2, left inferior frontal junction; 3, right inferior frontal junction; 4, mPFC; 5, PCC.

information was constant across all three conditions; only task goals were manipulated. A similar pattern of activation was observed for the FFA (**Supplementary Fig. 2b**), except that suppression was not observed, consistent with previous findings[1] (**Supplementary Discussion**).

Functional connectivity maps were generated by correlating trial-by-trial variation in activity from the PPA and FFA with every other voxel in the brain[3,14]. Enhancement and suppression networks were derived by differentially pairing these visual cortical seed regions with a condition and then contrasting the maps with those obtained by pairing the seeds with the passive viewing condition. For example, an enhancement network was generated by contrasting PPA connectivity for SM-O > PV-O and a suppression network by contrasting PPA connectivity for FM-O > PV-O.

Analysis revealed that the enhancement network, independent of the visual cortical region that served as a seed, included brain regions of the FPN[8,9], notably the right middle frontal gyrus and bilateral inferior frontal junction (**Fig. 2a**,**b** and **Supplementary Table 1**). In contrast, the suppression networks included regions of the default network[9,11], notably the medial prefrontal cortex (mPFC) and posterior cingulate cortex (PCC) (**Fig. 2c**,**d** and **Supplementary Table 2**). The suppression network regions were largely distinct from those identified in the enhancement network, as confirmed by a direct contrast between the networks (**Fig. 2e**,**f** and **Supplementary Table 3**). It was verified that suppression network regions were nodes of the canonical default network by a whole-brain conjunction analysis between the suppression networks and the default network derived using an independent task (**Supplementary Methods** and **Supplementary Fig. 3**). Further analysis of default network regions of interest derived from the localizer task (specifically, the mPFC and PCC) indicated that these regions were differentially coupled with visual cortical regions based on task goals, that is, greater functional connectivity when activity in visual regions were being suppressed (**Supplementary Fig. 4**). Moreover, analysis revealed that the differential connectivity of stimulus-selective visual regions with the FPN and default network occurred simultaneously and switched dynamically with task goals. Notably, visual cortical coupling with default network required the presence of irrelevant information, that is, in conditions without task-irrelevant information (face memory and scene memory), but the same goals of remembering the face or scene, neither PPA nor FFA were functionally connected with default network regions (**Supplementary Fig. 5**).

Regression analyses revealed three important aspects of the relationship between functional coupling, activity modulation and performance. First, participants who demonstrated the strongest connectivity between the PPA and mPFC region of the default network during FM-O (relative to PV-O) were those who also showed the greatest PPA activity suppression (**Supplementary Fig. 6**). This neural-behavioral relationship was limited to the PPA, consistent with the finding that FFA was not suppressed. Second, trial-by-trial fluctuations in default network activity (particularly the mPFC and PCC) negatively correlated with response time on the delayed-recognition task ($P < 0.05$; **Supplementary Methods**), such that trials with the most reduced activity in these default network regions were those trials with the fastest response time. This is similar to previous findings that neural signatures of ignoring task-irrelevant stimuli are predictive of working memory performance[15]. Of note, this neural-behavioral relationship occurred only for tasks when irrelevant stimuli were present (**Supplementary Fig. 7**), consistent with functional connectivity being dependent on the presence of irrelevant information. Third, a converging result was obtained using an across-participant regression analysis of response time and functional connectivity (overlap versus non-overlap conditions), which revealed that greater PPA default network coupling (specifically, with the mPFC and PCC) was associated with greater resistance to the negative effect of distraction on working memory performance (**Supplementary Fig. 8**).

Our results indicate that sensory cortical regions are functionally connected with distinct large-scale neural networks based on task goals. Consistent with previous findings, the FPN was associated with top-down enhancement of task-relevant stimuli[3]. Our results also reveal that the default network is functionally connected with stimulus-selective visual cortex only in the presence of irrelevant information and that for the PPA this functional coupling is predictive of both the neural suppression of task-irrelevant information and resistance to the effect of distraction on working memory. This pattern of convergent results suggests that the network finding is functionally important. One interpretation is that suppression of externally generated distracting information (that is, suppression of visual cortical activity) is intimately coupled with the suppression of internally generated distracting information (that is, suppression of default network regions) (**Supplementary Discussion**). Although connectivity was also observed between the FFA and default network, it was not associated with significant suppression; the reason for this dissociation, as well as the generalization of this finding to other sensory areas, remains to be determined. Of note, fMRI data is correlational and mechanistic interpretations of causality will require the support of a direct perturbation approach, such as transcranial magnetic stimulation (**Supplementary Discussion**). In summary, our results reveal a previously unknown form of flexible, dissociable network dynamics between visual cortices and frontal and parietal regions based on task goals and the presence of irrelevant information.

Note: Supplementary information is available on the Nature Neuroscience website.

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AUTHOR CONTRIBUTIONS

J.Z.C. and A.G. designed the experiment. J.Z.C. collected and analyzed data. J.Z.C. and A.G. wrote the paper.

COMPETING FINANCIAL INTERESTS

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