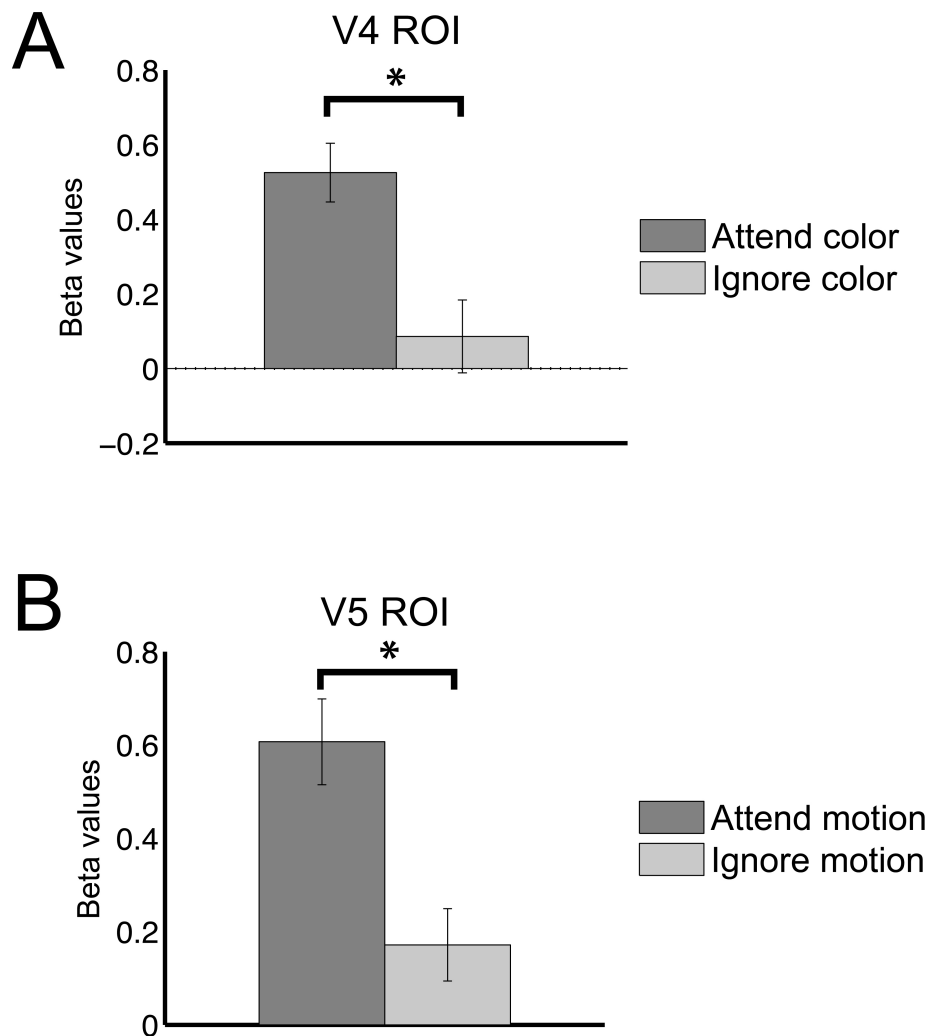


Causal role of the prefrontal cortex in top-down modulation of visual processing and working memory

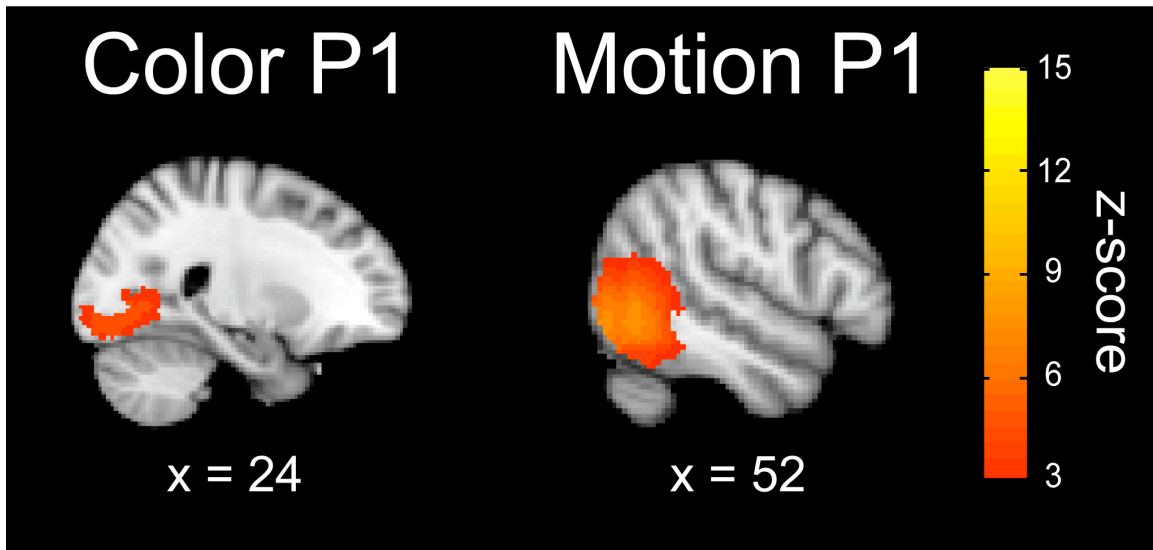
Theodore P. Zanto, Michael T. Rubens, Arul Thangavel, and Adam Gazzaley

Supplementary Fig. 1



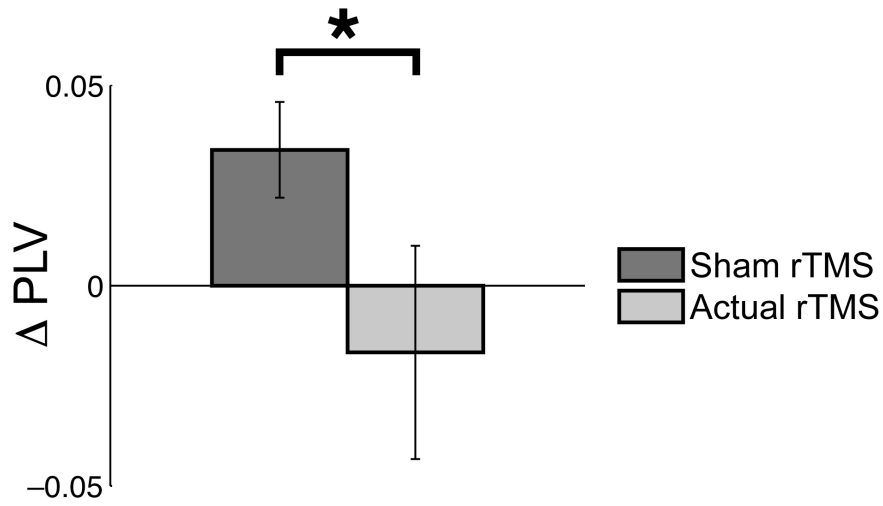
Supplementary Figure 1. Attentional modulation of BOLD fMRI signal for processing (a) color and (b) motion features in areas V4 and V5, respectively. Error bars represent s.e.m. Asterisk indicates $P < 0.0001$.

Supplementary Fig. 2



Supplementary Figure 2. Source localization of the P1 for color (left) and motion (right) stimuli. Regions include striate, extrastriate and inferior temporal regions. Notably, sources of the P1 from color stimuli includes V4 whereas sources of the P1 from motion stimuli encompasses V5.

Supplementary Fig. 3



Supplementary Figure 3. Change in alpha band phase locking values (attend – ignore) between right-frontal and central-posterior regions. Bar graph shows a decrease in PLV modulation following actual rTMS. Error bars represent s.e.m. Asterisk indicates $P < 0.05$.

Supplementary Table 1

	V4 connectivity: attend > ignore	x	y	z	Cluster size (mm³)
<i>Frontal cortex</i>	Left Inferior Frontal Gyrus / Frontal Pole	-38	30	8	9288
	Left Paracingulate Gyrus	-4	20	40	6968
	Right Inferior Frontal Gyrus	46	18	4	5128
	Right Frontal Pole	32	56	14	2248
	Right Superior Frontal Gyrus	18	36	40	1320
	Right Frontal Pole	20	48	-10	1224
	Right Inferior Frontal Junction	44	20	24	1128
	Right Frontal Eye Field	38	8	58	872
	Left Frontal Eye Field	-36	4	54	416
	Left Frontal Pole	-26	52	-14	216
<i>Parietal cortex</i>	Left Supramarginal / Angular Gyrus	-36	-52	42	2808
	Right Supramarginal / Angular Gyrus	44	-50	36	2352
	Right Superior Parietal Lobule	36	-70	52	1592
	Left Superior Parietal Lobule	-22	-62	66	1064
	Right Precuneus	8	-60	46	1032
	Right Superior Parietal Lobule	14	-70	62	680
	Left Postcentral Gyrus	-50	-22	48	304
	Right Superior Parietal Lobule / Postcentral Gyrus	30	-28	48	176

Supplementary Table 1. Summary of all fronto-parietal regions with functional connectivity to area V4 that may be involved in top-down modulation (i.e. attend > ignore; $P < 0.01$, corrected). Center-of-mass coordinates listed are in MNI space.

Supplementary Table 2

	V5 connectivity: attend > ignore	x	y	z	Cluster size (mm³)
<i>Frontal cortex</i>	Left Frontal Pole	-36	50	12	1808
	Left Frontal Eye Field	-22	0	60	1024
	Left Inferior / Middle Frontal Gyrus	-32	32	16	744
	Right Supplementary Motor Cortex	2	-2	60	368
	Right Inferior Frontal Junction	58	12	24	360
	Right Superior Frontal Gyrus	4	14	54	320
	Left Inferior Frontal Junction	-56	8	36	104
	Right Frontal Eye Field	10	10	70	104
<i>Parietal cortex</i>	Right Supramarginal Gyrus / Superior Parietal Lobule	34	-42	38	1632
	Left Superior Parietal Lobule	-8	-66	62	416
	Left Supramarginal / Postcentral Gyrus	-34	-38	42	408
	Left Inferior/Superior Parietal Lobule	-30	-48	60	384
	Left Inferior/Superior Parietal Lobule	-44	-42	58	368
	Right Supramarginal Gyrus	56	-30	52	240
	Right Superior Parietal Lobule	30	-50	58	144
	Right Precuneus	18	-62	22	96

Supplementary Table 2. Summary of all fronto-parietal regions with functional connectivity to area V5 that may be involved in top-down modulation (i.e. attend > ignore; $P < 0.01$, corrected). Center-of-mass coordinates listed are in MNI space.

Supplementary Results

First, a 1-back task was utilized during fMRI recording to localize each participant's V4 and V5 area, which then served as regions of interest (ROIs; see Methods for details). ROIs were restricted to the right hemisphere, as this hemisphere was previously shown to elicit greater responses for these features²⁴. In order to evaluate top-down modulation within the ROIs during the encoding period, data from the experimental task were submitted to a general linear model (GLM) for univariate analysis. Average beta values for each ROI were then submitted to a repeated measures analysis of variance (ANOVA) with ROI (V4 / V5) and feature relevance (attend / ignore). The utility of individual ROIs allows statistics to be calculated in each participant's native space. A main effect was observed for feature relevance, such that attended features elicit greater activity in the respective ROI ($F_{1,18} = 81.14$, $P < 0.001$). No other main effect or interaction was observed. To ensure each ROI was modulated by attention, paired t -tests between attended and ignored features were conducted separately for V4 and V5. In V4, attention to color elicited greater activity than ignoring color ($t_{18} = 3.82$, $P < 0.005$; **Supplementary Fig. 1a**), and in V5, attention to motion yielded greater activity than ignored motion ($t_{18} = 7.67$, $P < 0.001$; **Supplementary Fig. 1b**). These results reveal the neural signature of top-down modulation in both ROIs during the encoding period, and replicate the finding of a recent study using this paradigm in a separate cohort of participants²⁴.

Supplementary Discussion

The decision was made not have the participants return to the lab for a third session (second rTMS session) to assess a control brain region. Instead, a set of a priori predictions were formulated to serve as internal controls: effects of rTMS to the right IFJ on *both* top-down modulation and WM performance were predicted to be greater, 1) for color stimuli vs. motion stimuli, 2) in the first half of the experimental block vs. the second half, and 3) following actual rTMS vs. sham rTMS. All of these predictions were validated in the experiment for both modulation and performance, thus giving us confidence that these effects were generated as a result of perturbing function in the right IFJ by rTMS. Further support of this conclusion is provided by the relationship between functional connectivity and P1 modulation, which indicates that participants who utilized the right IFJ more for color processing were more susceptible to rTMS-induced decline in color-related P1 modulation. Additionally, participants who exhibited strong left IFJ-V5 functional connectivity in their V5 attend network did not show a rTMS-induced decline in P1 modulation, whereas weaker left IFJ recruitment resulted in diminished P1 modulation following rTMS during motion processing. Thus, the fMRI connectivity data proved valuable for more than guiding the target site for TMS, it directly informed our hypotheses.