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The visual attention network untangled

Sander Nieuwenhuis & Tobias H Donner

Goals are represented in prefrontal cortex and modulate sensory processing in visual cortex. A new study combines TMS, fMRI and EEG to understand how feedback improves retention of behaviorally relevant visual information.

How does the brain select the relevant visual information for access to short-term memory, while filtering out irrelevant information? It has long been hypothesized that this is the result of 'top-down' signals sent from prefrontal cortex (PFC) to visual cortex, where these signals bias visual processing[1–3]. Many studies have provided evidence consistent with this hypothesis by characterizing the modulations of neuronal activity within either PFC or visual cortex during visual attention tasks. However, a conclusive test of this hypothesis requires a direct assessment of the interaction between PFC and visual cortex during attention. Only recently has it become possible to directly probe such interactions in the working human brain. In this issue of *Nature Neuroscience*, Zanto *et al.*[4] use a versatile combination of techniques to characterize the interaction between PFC and visual cortex during a visual attention task.

The most conclusive demonstration of network interactions entails manipulating the activity in one brain region (for example, PFC) and measuring the remote effects in a putative interconnected region (for example, visual cortex)[5]. A seminal microstimulation study in monkeys set the stage for this powerful approach[6]. Stimulation of a specific population of neurons surrounding a microelectrode in the monkey frontal eye field, a PFC region involved in attention, exerts effects on neuronal activity in visual cortical area V4 that precisely mimic the effects of selective visual attention in V4 (ref. 6). Subsequent studies in the human brain have combined transcranial magnetic stimulation (TMS)—which perturbs neuronal processing in the brain region underneath the stimulation coil—with either functional magnetic resonance imaging (fMRI) or electroencephalography (EEG)[5]. In accord with the findings in monkeys, TMS over the human frontal eye field exerts remote effects on EEG and fMRI responses in the visual cortex[5].

In the new study by Zanto *et al.*[4], participants were instructed to attend to either the color or the motion direction of stimuli, ignore the irrelevant feature, and memorize the attended feature until the information was probed. The authors studied the effect of TMS over a task-relevant PFC control region on EEG measures of the attentional modulation in visual cortex and of the communication between PFC and visual cortex. Furthermore, to address the notion that attended stimuli have preferential access to short-term memory[7], the authors asked whether disrupting PFC activity with TMS—presumably interfering with attentional biasing signals—would affect short-term memory for attended stimuli. The study thus provides a comprehensive picture of the large-scale network mechanisms that afford feature-based attention.

Rather than relying on previous work to select a putative PFC region that exerts top-down control over visual cortex, the authors conducted a separate experiment to identify PFC regions involved in their specific task. So in stage 1 of the study (**Fig. 1**), participants performed the visual attention task during fMRI. The authors extracted the single-trial fMRI responses from two visual cortical regions known to process color (area V4) and motion (area V5, also known as MT) and searched for regions in association cortex in which fMRI responses correlated with these responses in visual cortex. For both V4 and V5, this analysis gave rise to a highly distributed network of potential control areas, comprising posterior parietal regions as well as PFC regions (for example, the frontal eye field). Consistent with previous work by the authors[8], another PFC region (in the junction between the inferior frontal sulcus and the precentral sulcus) showed the strongest overlap between the 'attention-to-color' and 'attention-to-motion' networks. This PFC region, a common node of the 'dorsal attention network'[9], was right-lateralized for attention to color and bilateral for attention to motion[8].

In stage 2 of the study (**Fig. 1**), the same participants received prolonged, repetitive TMS to the previously identified right PFC region. This TMS protocol typically disrupts neuronal processing in the underlying brain region for tens of minutes, thus inducing a temporary 'virtual lesion'. In stage 3, while the effects of TMS gradually wore off, the authors measured the resulting downstream effects on EEG and task performance. Prefrontal TMS reduced the P1 amplitude modulation, a stimulus-evoked EEG marker of top-down attention effects in the visual cortex[10]. It also impaired the accuracy of participants' short-term memory reports. These findings indicate that disrupting neuronal processing in one PFC region diminished top-down modulation of visual cortical activity during early encoding stages and impeded the entry of attended information into short-term memory. Of particular importance, the TMS effects on P1 and memory performance showed a highly specific pattern: they occurred only during the first half of the experiment—before the effects of TMS wore off—and only when participants attended to color, suggesting that attention to motion was compensated by the unaffected mirror area in the left PFC.

To further demonstrate the close relationship between top-down biasing signals from PFC, selective attention effects in visual cortex, and short-term memory for attended color stimuli, Zanto *et al.*[4] exploited individual differences in the corresponding fMRI, EEG and behavioral measures. Correlation analyses confirmed that participants with a stronger coupling between the critical PFC area and visual cortical area V4 (**Fig. 1**, stage 1) showed a stronger effect of prefrontal TMS (stage 2) on

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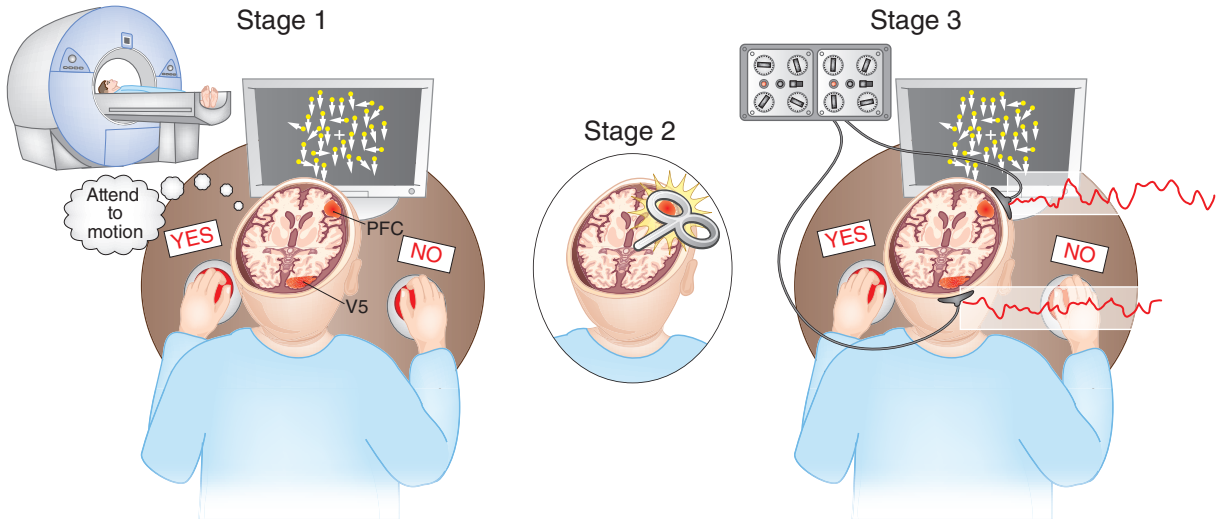

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Figure 1 Outline of the study by Zanto *et al.*[4]. In stage 1, participants were scanned while asked to attend to either the color or the motion of a series of stimuli, maintain these features in short-term memory for a delay of a few seconds, and then decide whether a subsequent probe stimulus matched the items held in memory. The investigators then searched for brain areas where task-related fMRI responses correlated with responses in both V4 (a proxy for color processing) and V5 (a proxy for motion processing)—and correlated more so when participants attended to the corresponding feature than when they ignored this feature. This analysis identified a right-hemisphere PFC region as a putative control region for top-down attentional modulation of color and motion processing. In stage 2, the same participants first received repetitive TMS of this PFC region to disrupt the putative top-down signals; controls received sham TMS. Immediately thereafter, in stage 3, EEG data were gathered while participants performed the same visual attention task as before. The investigators examined the effect of TMS on the attentional modulation of an early visual evoked potential component, the EEG phase coherence between PFC and visual cortex, and short-term memory performance.

attentional modulation of the P1 potential in visual cortex (stage 3); this, in turn, predicted a stronger detrimental effect of prefrontal TMS on visual short-term memory performance.

Recall that the authors defined the target region for TMS on the basis of its interaction—assessed with fMRI—with visual cortical areas V4 and V5. To characterize the mechanism of this interaction in more detail, they went on to explore the effect of prefrontal TMS on the phase coherence of EEG oscillations measured over frontal and visual cortex. Attention modulated long-range coherence before stimulus onset in the alpha (about 7–14 Hz) frequency range. Prefrontal TMS reduced this attentional modulation, again suggesting that the targeted PFC region interacts with visual cortex during top-down attention. However, the interpretation of coherence between brain regions based on scalp EEG measurements is complicated by potential volume-conduction artifacts. Therefore, this potentially important result remains to be replicated in future studies at the cortical source level, ideally in direct intracranial recordings.

The study by Zanto *et al.*[4] provides a showcase for how to combine tools in cognitive neuroscience to unravel the large-scale network interactions that underlie cognition in the human brain. For example, future studies could use this approach to address the question of how the neural systems affording attention and short-term memory are related to each other[7]. Zanto *et al.*[4] have pinpointed a PFC region required for the selection of relevant visual information during the encoding phase of the task. Is the same region also critical for the online maintenance of that information in short-term memory during the subsequent delay phase? Furthermore, studies of top-down attentional control have revealed the involvement of a whole network of regions distributed across the PFC and parietal cortex[3,9]. Zanto *et al.*[4] manipulated one of these control regions and characterized the remote effects in visual cortex. It remains unknown how specific these remote effects are for the target PFC region. Future direct comparisons between the remote TMS effects of different putative frontal and parietal control regions will be critical for dissecting the attention network of the human brain.

Long-range neuronal coherence in specific frequency bands may be critical for the effective communication between distant brain regions[11]. In line with the current study, a number of recent studies of visual attention in humans[12,13] (using magnetoencephalography combined with source reconstruction) and monkeys[14,15] (using invasive local field potential recordings) have demonstrated modulations of coherence between PFC and visual cortex. However, in the previous studies, attention affected long-range coherence in higher frequency bands—in particular, in the beta and gamma bands—than in the results of Zanto *et al.*[4]. It is unknown why the frequency bands of cortical long-range communication vary so much across tasks. More importantly, causal evidence for the functional significance of these diverse band-limited effects is missing. Combining detailed analyses of cortical long-range coherence with direct stimulation approaches will be critical for understanding the mechanisms of long-range communication in the brain.

COMPETING FINANCIAL INTERESTS
The authors declare no competing financial interests.

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