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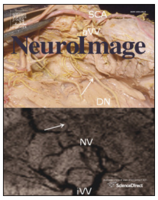

Review

Anticipatory alpha phase influences visual working memory performance

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ABSTRACT

Alpha band (8–12 Hz) phase dynamics in the visual cortex are thought to reflect fluctuations in cortical excitability that influences perceptual processing. As such, visual stimuli are better detected when their onset is concurrent with specific phases of the alpha cycle. However, it is unclear whether alpha phase differentially influences cognitive performance at specific times relative to stimulus onset (i.e., is the influence of phase maximal before, at, or after stimulus onset?). To address this, participants performed a delayed-recognition, working memory (WM) task for visual motion direction during two separate visits. The first visit utilized functional magnetic resonance (fMRI) imaging to identify neural regions associated with task performance. Replicating previous studies, fMRI data showed engagement of visual cortical area V5, as well as a prefrontal cortical region, the inferior frontal junction (IFJ). During the second visit, transcranial magnetic stimulation (TMS) was applied separately to both the right IFJ and right V5 (with the vertex as a control region) while electroencephalography (EEG) was simultaneously recorded. During each trial, a single pulse of TMS (spTMS) was applied at one of six time points (−200, −100, −50, 0, 80, 160 ms) relative to the encoded stimulus onset. Results demonstrated a relationship between the phase of the posterior alpha signal prior to stimulus encoding and subsequent response times to the memory probe two seconds later. Specifically, spTMS to V5, and not the IFJ or vertex, yielded faster response times, indicating improved WM performance, when delivered during the peak, compared to the trough, of the alpha cycle, but only when spTMS was applied 100 ms prior to stimulus onset. These faster responses to the probe correlated with decreased early event related potential (ERP) amplitudes (i.e., P1) to the probe stimuli. Moreover, participants that were least affected by spTMS exhibited greater functional connectivity between V5 and fronto-parietal regions. These results suggest that posterior alpha phase indexes a critical time period for motion processing in the context of WM encoding goals, which occurs in anticipation of stimulus onset.

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Introduction

Working memory (WM) for visual motion information is critical for everyday activities, such as when trying to cross a busy street. This scenario requires maintaining memory traces of vehicular motion in one direction, while traffic in the other direction is assessed. Despite its important function, the neural basis of motion-based WM encoding is still unclear. To understand how the brain encodes visual motion into WM, two fundamental questions must be answered: which neural regions are involved and when is their involvement critical for performance? Important steps along this path have been accomplished by studies exploring the localization of cortical processing in response to viewing motion stimuli. Neuroimaging has revealed that area V5/hMT+, within the medial temporal lobe, shows a selective response to visual motion (Culham et al., 2001; Schoenfeld et al., 2007; Zeki et al., 1991). Although the location of V5 is well defined, the role of higher cognitive regions that influence V5 processing is still unclear, as well as when are the critical processing time periods relative to stimulus onset.

To assess the timing of visual cortical processes, studies using electroencephalography (EEG) and magnetoencephalography (MEG) have often focused on posterior alpha band oscillations between 8 and 12 Hz, which characterizes both suppression and timing of attentional processes involved in selection of stimulus representations (Freunberger et al., 2009; Klimesch, 2012). Interestingly, it has been found that the phase of ongoing alpha band oscillations reflects fluctuations in visual cortical excitability, such that stimuli presented during the peak (maximum amplitude) of the alpha oscillation are better detected than stimuli that appear during the trough (minimum amplitude) (Busch et al., 2009; Mathewson et al., 2009; Zauner et al., 2012). Consistent with this, the effects of transcranial magnetic stimulation (TMS) are known to be contingent on oscillatory parameters (Rubens and Zanto, 2012), including the alpha phase when a TMS pulse is applied. For example, a single pulse of TMS (spTMS) to the occipital cortex is more likely to evoke a phosphene when applied during peak alpha phase (Dugue et al., 2011) and neural entrainment to 10 Hz-TMS (i.e., alpha-like) is highest when TMS onset coincides with peak alpha phase (Thut et al., 2011). Importantly, these results indicate that perception may be oscillatory in nature, affording temporal windows of optimal opportunity to process information from the environment. Therefore, we hypothesized that perturbing visual cortical activity at specific phases of the ongoing alpha rhythm would differentially alter WM for motion direction.

Although it is reasonable to hypothesize that motion WM may be contingent upon the phase of ongoing alpha oscillations, a plethora of previous research has revealed the importance of the timing of spTMS relative to stimulus onset for motion processing. These studies utilized spTMS to transiently alter V5 activity at various times relative to motion stimuli onset and assess motion detection performance. Results indicated that spTMS to V5 can disrupt motion processing when applied prior to motion onset (−150–0 ms post onset) (Beckers and Zeki, 1995; Laycock et al., 2007; Maus et al., 2013; Sack et al., 2006; Stevens et al., 2009), near motion onset (0–50 ms post onset) (Beckers and Homberg, 1992; Beckers and Zeki, 1995; Laycock et al., 2007; Maus et al., 2013), and following motion onset (80–200 ms post onset) (Anand et al., 1998; Bosco et al., 2008; Laycock et al., 2007; Maus et al., 2013; Sack et al., 2006; Silvanto et al., 2005; Stevens et al., 2009; Walsh et al., 1998). These results suggest that multiple temporal windows are critical for motion processing. Thus, the effects of spTMS on motion WM performance may be contingent on both alpha phase at the time of the TMS pulse, as well as the specific time of the pulse relative to stimulus onset.

It has also been proposed that critical motion processing time periods arise not solely based on intrinsic V5 activity, but via interactions of distributed, fronto-parietal networks that transmit top-down signals to V5 (Laycock et al., 2007). This is highly plausible given the role of fronto-parietal regions both during periods of stimulus expectation (i.e., prior to the stimulus onset) (Bollinger et al., 2010; Carlsson et al., 2000; Coull and Nobre, 1998) and early sensory processing (Foxe and Simpson, 2002; Ruff et al., 2006; Silvanto et al., 2006; Zanto et al., 2011b). We have previously shown that WM for motion direction is associated with modulation of activity in V5 that is dependent on functional connections between V5 and fronto-parietal regions subserving attention and memory processes (Zanto et al., 2010a, 2011b). Specifically, a region within the prefrontal cortex, the inferior frontal junction (IFJ), was shown to be consistently engaged across individuals and causally involved in modulating neural activity in visual cortex during WM encoding at the P1 (100 ms post stimulus onset) of the event related potential (ERP). In addition to the attention based, or top–down, modulation of the P1 to motion stimuli, it is interesting to note that the P1 may be generated, at least in part, by alpha band oscillations (Freunberger et al., 2008). Therefore, we hypothesized that spTMS targeting V5 and IFJ would impact WM performance, as well as the P1 amplitude, based on the posterior alpha phase at the time of TMS pulses, and that the time relative to stimulus onset would interact with this influence of phase.

To address our hypothesis, a delayed recognition task for motion direction was used in two separate experimental sessions (Fig. 1A). Guided by the results from previous studies (Zanto et al., 2010a, 2011b), the

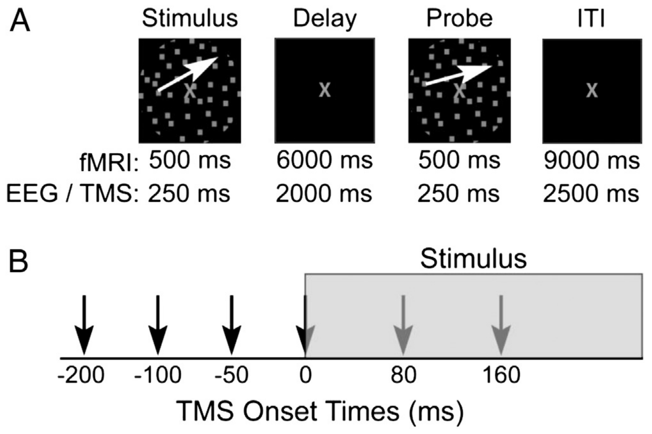

Fig. 1. Experimental paradigm. (A) Delayed recognition task for motion direction. White arrows depict the direction of motion and were not present during the experiment. (B) Timing of spTMS onsets relative to the onset of the stimuli to be remembered. Note: only one TMS pulse was applied per trial.

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