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Letter to the Editor

A disruption of colour priming following continuous theta burst transcranial magnetic stimulation

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It is well established that the presentation of one visual attribute (e.g., colour, motion) can improve the likelihood of the same attribute being detected on a subsequent trial (Tulving and Schacter, 1990). There is growing evidence to suggest that this effect is driven in a bottom-up manner (Maljkovic and Nakayama, 1994), which is dependent upon functionally specialized extrastriate regions (Walsh et al., 2000; Campana et al., 2002; Kristjánsson et al., 2005, 2007). For example, lesions to macaque area V4 and TEO abolish colour and form priming (Walsh et al., 2000). Also, in humans, transcranial magnetic stimulation (TMS) targeted at V5/MT has been shown to abolish motion priming (Campana et al., 2002). However, there is also evidence that relatively minor manipulation of the stimuli can alter the level at which priming seems to occur (see Kristjánsson and Campana, 2010). For example, lower visual levels can mediate motion priming when a prime of the same type as the probe stimulus is used, whereas priming occurs at a higher level when the prime and probe differ in type (Campana et al., 2008).

Here, we sought to establish the effects of continuous theta burst TMS (cTBS; Huang et al., 2005) targeted at human left V4 (Morita et al., 2004), left V5/MT or the vertex, on the perceptual priming of colour. Based on the assumption that colour priming is a consequence of neural activity in colour selective extrastriate regions, we expected that cTBS targeted at human V4 would disrupt colour priming, but that this would not occur following cTBS to our active control sites (V5/MT and the vertex).

Eighteen participants (six per stimulation group) completed a colour priming paradigm (Fig. 1a) prior to (baseline) and following cTBS targeted at human V4, V5/MT or the vertex. During the task, participants were presented with a coloured (red or green) or achromatic grapheme, which acted as a congruent, incongruent, or neutral condition (achromatic grapheme trials). After participants had read the grapheme aloud, they were presented with three coloured diamonds (either red or green) each missing either the left or the right side (Fig. 1a). Two of the diamonds were the same colour and one was odd. The participants' task was to indicate which side of the odd coloured diamond was missing.

Stimulation was delivered via a figure of eight coil with a 70 mm diameter using a Magstim Super Rapid Stimulator (Magstim, UK). An offline cTBS paradigm was used (see Banissy et al., 2010 for TMS parameters). Locations for cTBS were identified using Brainsight TMS-magnetic resonance coregistration system (Rogue Research, Montreal, Canada). The left V4 site was selected based on coordinates from neurologically normal participants in an functional magnetic resonance imaging (fMRI) study investigating colour perception (36, −56, −14; Morita et al., 2004). The coordinates for V5/MT (44, −67, 0) were the averages of neurologically normal participants in an fMRI study of motion processing and were confirmed functionally through phosephenes (Dumoulin et al., 2000). The vertex was identified as the point midway between the inion and the nasion, equidistant from the left and right intertragal notches.

As per previous perceptual priming studies (Walsh et al., 2000; Campana et al., 2002; Kristjánsson et al., 2005, 2007), we expected participants to respond faster to the odd coloured diamond when this was congruent with the prime grapheme. This was found to be the case in all baseline conditions [V4 group: $t(5) = 3.07$, $p = .028$; V5/MT group: $t(5) = 2.94$, $p = .032$; Vertex group: $t(5) = 4.67$, $p = .005$] and the size of the priming effect (i.e., incongruent stimulus median reaction time minus

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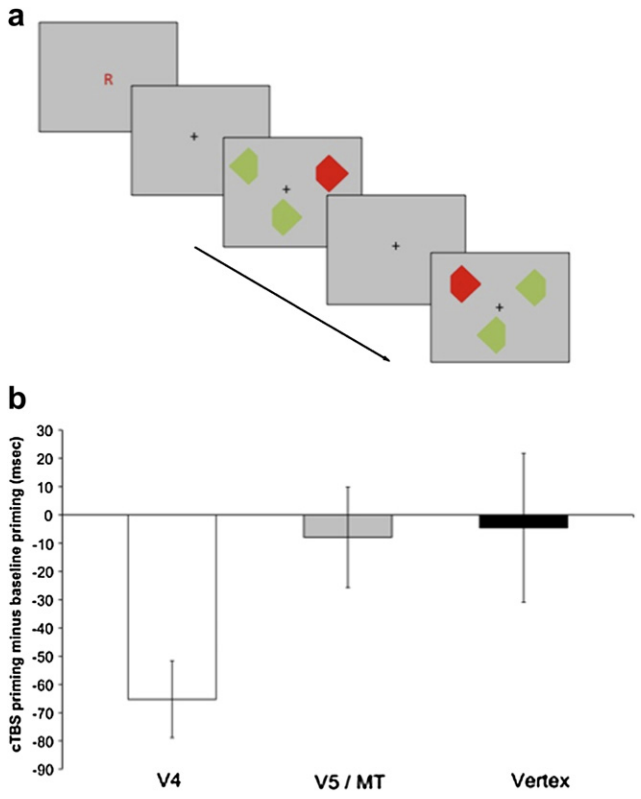

Fig. 1 – (a) Summary of task protocol. During the task participants were presented with a fixation cross (1000 msec), followed by a coloured (red or green) or achromatic grapheme, which remained on screen until participants read the grapheme aloud. The grapheme acted as a congruent, incongruent, or neutral condition (achromatic grapheme trials) and the following graphemes were used in a random order across participants (the same set of graphemes were used in the pre and post TMS conditions for each participant): W, T, X, V, P, Z, T, R, D, M, G, C, E, S, J, K, L. After participants had read the grapheme aloud they completed two trails in which they were presented with a fixation cross (1000 msec), followed by three coloured diamonds (either red or green) each missing either the left or the right side. Two of the diamonds were the same colour and one was odd. The participants' task was to indicate which side of the odd coloured diamond was missing and the stimuli remained on screen until the participant responded with a key press. On each trial the odd coloured diamond was either the same colour as the coloured grapheme prime (congruent trials; 36 trials in total); differed from the chromatic grapheme (incongruent trials; 36 trials in total); or all diamonds differed from the achromatic grapheme (neutral trials; 36 trials in total). (b) Difference between the size of the priming effect in the post cTBS and pre-cTBS conditions for each site stimulated. A disruption in reaction times following stimulation is shown by a negative value.

congruent stimulus median reaction time) was similar across sites [$F(2, 15) = 1.70$, $p = .216$].

To examine the effects of cTBS on priming, we firstly compared the size of the colour priming effect (incongruent reaction time minus congruent reaction time) in the baseline condition with the size of the colour priming effect following cTBS to each site separately by using paired t-tests. This revealed that cTBS to V4 [$t(5) = 4.59$, $p \leq .01$], but not MT/V5 [$t(5) = .446$, $p = 0.67$] or the vertex [$t(5) = .174$, $p = 0.87$], reduced colour priming. To ensure that this effect was not due to ceiling effects in reaction time or accuracy following V4 stimulation we also compared accuracy and overall reaction time performances at baseline and following cTBS in the V4 group. This revealed no significant effect on accuracy performance [$t(5) = .349$, $p = .741$]. There was a significant facilitation of overall reaction times following V4 stimulation [Baseline mean ± s.e.m = 612 ± 38.81; V4 TMS mean ± s.e.m = 565.75 ± 36.57; $t(5) = 6.36$, $p = .001$], but importantly the reaction time in the V4 TMS condition was not at ceiling and is in line with previous effects seen with online TMS priming studies (Campana et al., 2002, 2008).

Having determined within site effects, we then compared the magnitude of reduction in colour priming across sites by calculating the difference between the sizes of the priming effect in the post cTBS conditions relative to baseline for each group using a between subjects *t*-test. This showed that there was a significant disruption in colour priming following cTBS to human V4 relative to MT/V5 [$t(10) = 2.52$, $p = .015$, one-tailed] and relative to the vertex [$t(10) = 2.029$, $p = .035$, one-tailed], but that the effects of stimulation to MT/V5 and the vertex did not differ from one another [$t(10) = -.105$ $p = .918$; Fig. 1b].

These findings demonstrate a site specific disruption in colour priming following cTBS and are consistent with the notion that the perceptual priming of visual attributes relies upon neural activity in functionally specialized regions of the visual cortex (Tulving and Schacter, 1990). They parallel findings that macaques show deficits in colour priming following lesions to macaque area V4 (Walsh et al., 2000) and extend findings that neural activity in human MT/V5 is crucial for motion priming in humans (Campana et al., 2002), by showing that other functionally specialized extrastriate regions play a critical role in perceptual priming for healthy adults. It should be noted, however, that while we have shown a disruption of colour priming by stimulating previously reported coordinates for V4, the V4 site is on the ventral surface of the cortex and likely to be at the limits of the depth of human brain stimulation. However, in light of the expected functions of the nearby cortical regions, the most parsimonious explanation of the data obtained is that the effects were due to disruption of area V4/regions involved in colour processing rather than more superficial regions. Future studies may clarify this.

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