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The mental number line modulates visual cortical excitability

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ABSTRACT

The mental number line has been shown to exert an influence on the visuo-spatial allocation of attention, with presentation of numbers from the low and high ends of the mental number line inducing covert shifts of spatial attention to the left and right side of visual space, respectively. In the present study we used transcranial magnetic stimulation (TMS) to investigate whether this attentional modulation influences excitability of the early visual cortex. By using the phosphene threshold as a measure of visual cortical excitability, we show (in 10 subjects) that number priming modulates excitability of the early visual cortex in a topographic fashion: low numbers, associated with left side of space, increase the excitability of the right early visual cortex (the stimulation of which induces phosphenes in the left hemifield) and decrease the excitability of the left early visual cortex (the stimulation of which induces phosphenes in the right hemifield). The opposite pattern of results was observed for high numbers. Our results suggest that the attentional shifts induced by the mental number line are manifested at the earliest cortical stages of visual processing.

Numbers have been proposed to be represented along a horizontal left-to-right oriented mental number line, with small numbers lying on its left and high numbers on its right portion (e.g. [10,17]; for review [14]). A number of studies have supported this view. For example, subjects are usually faster in responding to low numbers with left-hand responses compared to right-hand responses, and faster in responding to high numbers with their right hand than with their left hand (the SNARC effect [10]). Interestingly, the putative mental number line does not only influence overt spatial responses but it also exerts an effect on the automatic allocation of spatial attention prior to any explicit response. Fischer et al. [12] found that exposure to low numbers (1 or 2) preceding the presentation of the target stimulus in a simple visual detection task facilitated detection of target appearing in the left hemifield, while exposure to high numbers (8 or 9) facilitated target detection in the right hemifield (see also [28]).

Several neuroimaging studies have implicated the intraparietal sulcus (IPS) and the angular gyrus (ANG) in the posterior parietal cortex (PPC) in numerical cognition [7,18,19,32] (for reviews, see [2,9,20]). This view is also supported by studies using transcranial magnetic stimulation (TMS) [5,13,23,24]. More recently, we have shown that the PPC plays a causal role in attentional shifts induced by the mental number line [6]. Given the interaction between numbers and space (e.g. [12]), a question that arises is whether the attentional impact of the mental number line on the allocation of visuo-spatial attention (mediated by the parietal cortex; cf. [6]), is reflected at the level of visual cortex. This possibility is supported by the finding that visual cortical excitability is affected by attentional shifts in the Posner paradigm [1]. Specifically, Bestmann et al. [1] showed recently that a lower TMS intensity was needed to elicit a phosphene when its apparent spatial location was attended, rather than unattended, demonstrating that spatial attention can enhance early visual cortical excitability. The objective of the present study was therefore to investigate, using TMS-induced phosphenes as a measure of visual cortical excitability (e.g. [8,21]), whether attentional shifts induced by the perception of numbers modulates the excitability of the visual cortex. Specifically, we investigated whether the proportion of trials on which phosphenes are induced from the left or right visual cortex is modulated by the presentation of numbers from either low or high ends of the mental number line.

Ten healthy (6 males and 4 females, mean age 28 years) took part in the investigation. All had normal or corrected-to-normal vision and had no history of mental or neurological illnesses. All participants had previously taken part in other TMS experiments in which they had reported clear phosphene perception in a well-circumscribed location, with eyes open, at 90% of TMS stimulator output or less. Nonetheless, they were all completely naïve to the scope of the current experiment. The study was approved by

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the local ethical committee and all subjects gave informed consent. Subjects were treated in accordance with the Declaration of Helsinki.

The sites for stimulation were located using a functional method typically used in studies investigating phosphenes [3,4,25,27] (see [31], for a detailed discussion). The stimulators used were two Magstim TM model 200 (Super-Rapid Magstim, Whitland, Dyfed) that generate a biphasic pulse; each stimulator was connected to a figure of eight coil with external diameters of 50 mm and created a peak magnetic field of approximately 2 T. Single pulses of TMS were delivered over the posterior occipital lobe in the vicinity of the midline over the back of the head, immediately superior to the inion, at 70–80% of maximum machine output. The coil position was adjusted until locations were stimulated that gave rise to unilateral phosphenes appearing in the left and right hemifield at an eccentricity of beyond 10 degrees of visual angle. As a result, two posterior occipital stimulation sites were selected for each subject: (1) left lateral posterior occipital (inducing phosphenes in the right hemifield); (2) right lateral posterior occipital (inducing phosphenes in the left hemifield). The scalp coordinates of these two sites ranged from 1–2 cm superior and 3–4 cm lateral from the inion. These coordinates are most likely to correspond to V2/V3 (e.g. [15]). We refer to these stimulation sites as left and right visual cortex. Coil orientations for all stimulations were such that the handle was horizontal and pointing away from the midline. Stimulation was carried out using 50-mm figure-of-eight coils. Both phosphene site localization and testing took place in a darkened room with the subjects keeping their eyes open fixated at a dark computer screen. For each subject the phosphene threshold was defined using a modified binary search algorithm (MOBS [30]; see also [29]), an adaptive threshold-finding algorithm. In this procedure, the TMS intensity is increased or decreased according to the subject's report on the previous trial. The upper boundary of the stimulation was 100% of stimulator output, and the lower limit 0% (i.e. the initial TMS intensity was 50%). Depending on the subject's report, either the upper boundary is decreased or the lower boundary is increased. This is repeated until the upper and lower boundary are within 2% of each other. The number of trials required for setting a threshold depends on the consistency of the subject's reports and in this experiment was between 10 and 18 trials. Mean phosphene thresholds, expressed as percentage of machine output, for the two stimulation sites were almost identical (left visual cortex: 71.8%, SD = 5.5; right visual cortex: 73.5%, SD = 6.4). Phosphene thresholds were re-measured at the end of testing; the post-testing values were 73.1% (SD = 6.7) and 75% (SD = 6.1). In the main experiment, both sites were stimulated at phosphene threshold.

On each trial, prior to phosphene induction, subjects were primed by a number digit from either the low (digits 1 or 2) or the high (digits 8 or 9) end of the mental number line. As a control, an asterisk was presented as a prime. The primes (digits and asterisk) were randomly presented across trials on a 24-inch screen. The viewing distance was 40 cm. Each trial began with a dim, gray fixation cross appearing in the center of the screen on a black background for 1000 ms. This was followed by a blank (black) screen for 500 ms, after which the prime was presented at fixation on the black background. The prime, a dim gray digit, had a height and width of approximately 0.8 and 0.4 degrees of visual angle, respectively. After the prime, the screen went black for 500 ms after which a TMS pulse was triggered either over the left or right visual cortex (two coils were placed over the subjects' head throughout the experiment; one over the left and the other over the right visual cortex). Whether it was the left or right visual cortex that was stimulated on a given trial was determined randomly by the computer software. After each TMS delivery, subjects pressed a button to report whether or not they had perceived a phosphene, and whether they had perceived in the left or right hemifield. Phosphenes induced by left and right visual cortical TMS always appeared in the right and left visual hemifield, respectively. There was a gap of 5 s between each trial.

There was a total 6 experimental conditions:

(1) Left visual cortex TMS and Low Number Prime.
(2) Left visual cortex TMS and High Number Prime.
(3) Left visual cortex TMS and Control (asterisk) Prime.
(4) Right visual cortex TMS and Low Number Prime.
(5) Right visual cortex TMS and High Number Prime.
(6) Right visual cortex TMS and Control (asterisk) Prime.

For each condition, 60 trials were completed for each subject (i.e. there were a total of 360 trials for each subject). The experiment was divided into 3 blocks of 120 trials. Within each block, all types of trials were intermixed. There was a 2-min break between each block. After each trial, subjects were asked to indicate, with a button press, whether (a) they perceived a phosphene in the left visual field; (b) they perceived a phosphene in the right visual field; or (c) they perceived no phosphene. Response time was unlimited. Subjects were explicitly and repeatedly instructed to avoid eye movements during the experiment and to maintain fixation at the center of the screen where all the primes appeared.

A 2×3 ANOVA, with TMS Site (left visual cortex, right visual cortex) and Prime Condition (Low Prime, High Prime, Control Prime) was carried out on the proportion of trials on which a phosphene was perceived. Mauchly's test indicated that the assumption of sphericity had been violated for the Prime by TMS Site interaction ($\chi^2(2) = 6.63$, $p = 0.036$), therefore degrees of freedom were corrected using Greenhouse–Geisser estimates of sphericity ($\varepsilon = 0.64$). The analysis indicated a significant interaction ($F(1.28, 11.52) = 19.4$; $p = 0.001$). Neither TMS site nor Prime Condition *per se* were significant.

Fig. 1 shows the frequency of phosphene perception for left and right visual cortex as a function of each priming condition.

Post hoc pair-wise comparisons revealed that when TMS was applied over the left visual cortex high number primes increased the frequency of phosphene perception in comparison to the control prime condition ($t(9) = 3.24$; $p = 0.01$); in contrast, low number primes decreased the frequency of phosphene perception relative to the control prime condition ($t(9) = 3.09$; $p = 0.013$).

Post hoc pair-wise comparisons revealed that when TMS was applied over the right visual cortex high number primes decreased the frequency of phosphene perception in comparison to the control prime condition ($t(9) = 3.34$; $p = 0.009$); in contrast, low number primes increased the frequency of phosphene perception relative to the asterisk prime condition ($t(9) = 4.29$; $p = 0.002$).

Our results show that the presentation of numbers from the low and high ends of the mental number line influence visual cortical excitability in a topographic-specific fashion. The presentation of a number from the low end of the mental number line increased the proportion of trials on which phosphenes were induced from stimulating the right visual cortex, indicating an increase in visual cortical excitability. In contrast, the presentation of high numbers reduced the proportion of trials on which phosphenes were induced from the right visual cortex, indicating a decrease in excitability. The opposite pattern was observed for phosphenes induced from stimulating the left visual cortex: the presentation of a high number increased the proportion of trials on which phosphenes were perceived, whereas low numbers reduced the proportion of such trials. As phosphenes induced from the right visual cortex appear in the left hemifield, and phosphenes induced from the left visual cortex appear in the right hemifield, this pattern of results is consistent with the view that small and large numbers

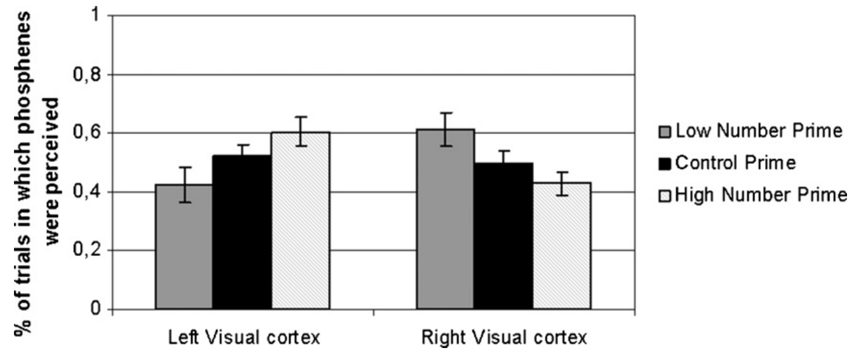

Fig. 1. The mean percentage of trials, as a function of the Number Prime condition, on which phosphenes were induced from the left and right visual cortex (average of 10 subjects). When TMS was delivered over the left visual cortex, presentation of numbers from the high end of the mental number line facilitated phosphenes perception whereas presentation of low numbers reduced phosphenes detection relative to the Control condition (in which an asterisk was presented as a prime). When TMS was delivered over the right visual cortex, presentation of numbers from the high end of the mental number line impaired phosphenes perception whereas low numbers facilitated phosphenes detection relative to the Control. Error bars represent standard deviations.

are associated with the left and right side of space, respectively [10,14,17].

The posterior parietal cortex (PPC) is a likely source of this modulation of visual cortical excitability by the mental number line. In a previous study [6] we showed that TMS applied over the left and right PPC abolished the effect of number priming on perception of external space in a line bisection task when applied between the prime and the line. Furthermore, previous studies have shown that the PPC plays a critical role in visual cortical top-down modulation. In a study by Silvanto et al. [26], TMS was used to induce activity in the PPC and phosphenes induced from V1/V2 provided a measure of excitability of the early visual cortex. The results showed that stimulation of PPC leads to a decrease in the intensity of stimulation required to elicit a visual percept implying that PPC TMS modulates excitability of the visual cortex. Similarly, using combined fMRI and TMS, Ruff et al. [22] showed that TMS applied over the PPC modulates the BOLD signal measured in the early visual cortex.

It has been demonstrated that number magnitude processing may be accompanied by an ocular motor orienting response [16]: in particular, processing of a large number followed by a small number was found to be accompanied with leftward eye movements, a tendency less pronounced or even reversed for the processing of a small number followed by a large number [16]. Moreover, visual activations in early visual cortical areas are found predominantly in the hemisphere contralateral to the fixation, even for small gaze shifts into one visual hemifield [11]. Therefore, one can in principle hypothesize that increases in visual excitability in our study were due to gaze shifts induced by numbers magnitude. However, our participants were instructed to keep fixation at the center of the screen throughout the experiment. Hence, our results are better explained by hypothesizing that numbers magnitude modulated spatial attention, and that these *covert* spatial attention shifts induced specific changes in the excitability of left and right visual cortex, according to previous reports [1].

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