Salience Representation in the Parietal and Frontal Cortex

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Abstract

■ Some objects in the visual field are more likely to attract attention because they are either intrinsically eye catching or relevant in the context of a particular task. These two factors, known as stimulus-driven and goal-directed factors, respectively, are thought to be integrated into a unique salience map, possibly located in the frontal or the parietal cortex. However, the distinct contribution of these two regions to salience representation is difficult to establish experimentally and remains debated. In an attempt to address this issue, we designed several dual tasks composed of a letter reporting task and a visual search task, allowing us to quantify the salience of each visual item by measuring its probability to be selected by attention. In Experiment 1, the salience of the visual search items depended on a combination of conspicuity and relevance factors, whereas in Experiment 2, stimulus-driven and goal-directed factors were tested separately. Then, we used transcranial magnetic stimulation to interfere transiently with the function of the right angular gyrus (ANG) or right FEFs in healthy subjects performing these dual tasks. We found that interfering with the ANG and the FEF function specifically altered the influence of salience on the letter report rate without affecting the overall letter reporting rate, suggesting that these areas are involved in salience representation. In particular, the present study suggests that ANG is involved in goal-directed salience representation, whereas FEF would rather house a global salience map integrating both goal-directed and stimulus-driven factors. ■

INTRODUCTION

The visual environment confronts us with a continuous flow of information that has to be processed as rapidly and as efficiently as possible. Many elements in this flow of information are worthless or irrelevant, but some of them, because they move quickly, are bright or colorful, or show resemblance with an object we are looking for, will attract our attention. When selected, these items will be processed more efficiently by our visual system because more neural resources will be allocated to treat them (Shaw & Shaw, 1977). Attentional selection is based on *salience* (Findlay & Walker, 1999; Gottlieb, Kusunoki, & Goldberg, 1998) resulting from the combination of these different features, although other terminologies have been used (Fecteau & Munoz, 2006). Two types of salience factors are typically identified: (a) stimulus-driven factors (Nothdurft, 1993) related to the physical characteristics that make a stimulus conspicuous (e.g., luminance, color, etc.) and (b) goal-directed factors that are task dependent (Navalpakkam & Itti, 2005; Posner, Snyder, & Davidson, 1980). In most instances, goal-directed factors override stimulus-driven factors, allowing us to select only the visual items that are pertinent to the task at hand, without being distracted by irrelevant conspicuous objects (Leber & Egeth, 2006; Bacon & Egeth, 1994; see, however, Schreij, Owens, & Theeuwes, 2008; Theeuwes, 2004).

These two types of salience factors are thought to be combined into a unique salience map (Itti, Koch, & Niebur, 1998; Koch & Ullman, 1985), although alternative hypotheses have been proposed (VanRullen, 2003; Li, 2002). Several brain areas have been regarded as potential neural substrates for salience maps, namely, the lateral intraparietal area (Gottlieb, 2007; Gottlieb et al., 1998) and Area 7a (Constantinidis & Steinmetz, 2005) in monkeys and the angular gyrus (ANG), intraparietal sulcus, and temporoparietal junction (Corbetta & Shulman, 2002; Yantis et al., 2002) in humans. The FEFs are also considered as a possible location for salience maps (Thompson, Bichot, & Sato, 2005) and other brain structures, such as the superior colliculus (Krauzlis, Liston, & Carello, 2004), and the pulvinar (Robinson & Petersen, 1992) might also be involved in salience representation. Because, by definition, salient stimuli are also more likely to attract attention, it remains, both conceptually and experimentally, difficult to differentiate attention and salience representations, and none of the previous human studies have clearly identified the distinct contribution of the aforementioned structures to attentional shift control and/or to salience representation.

Previous transcranial magnetic stimulation (TMS) studies have shown that interfering with the right ANG and FEF function altered the performance of cueing and visual search (VS) tasks (Muggleton, Cowey, & Walsh, 2008; Rushworth & Taylor, 2006; Chambers, Payne, Stokes, & Mattingley, 2004; Ellison, Rushworth, & Walsh, 2003; Muggleton, Juan, Cowey, & Walsh, 2003; Grosbras & Paus,

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2002; Walsh, Ellison, Ashbridge, & Cowey, 1999). However, because in these studies the cue salience was always identical, it remains impossible to determine whether the performance decrease in cueing tasks caused by ANG or FEF TMS was due to impaired attentional shifts or to a reduction in the cue salience. Similarly, in VS tasks, the longer RT and decrease in detection performance induced by TMS can be interpreted in different ways (Muggleton et al., 2008), and the possibility that TMS applied over ANG or FEF may have altered salience representations, affecting therefore the normal guidance of attention toward relevant items (Wolfe, Cave, & Franzel, 1989), has never been investigated experimentally.

To address this issue, we used TMS to disrupt neural processing in either the right ANG or the right FEF in healthy subjects performing a VS task in which the salience of each individual item was precisely measured. We chose to investigate these two areas in the right hemisphere only because the dominance of this hemisphere in attentional tasks has already been clearly established (Hodsoll, Mevorach, & Humphreys, 2008; Muggleton et al., 2003, 2006, 2008; Fierro et al., 2006; Fierro, Brighina, Piazza, Oliveri, & Bisiach, 2001; Ashbridge, Walsh, & Cowey, 1997). It is noteworthy, however, that the left parietal and frontal cortex might also be involved in salience computation. For instance, some authors have demonstrated the involvement of the left intraparietal sulcus region in the selection of global versus local shapes as a function of their stimulus-driven salience (Mevorach, Shalev, Allen, & Humphreys, 2008), suggesting a possible contribution of some left cortical regions to the guidance of spatial attention.

The present study comprises two experiments. In Experiment 1, participants had to report letters briefly flashed inside VS items while performing simultaneously a standard covert VS task (see Materials and methods and Figure 1; Zenon, Ben Hamed, Duhamel, & Olivier, 2008). The performance in the letter reporting task allowed us to determine, a posteriori, the attentional allocation according to the salience of VS items. In Experiment 2, participants had to perform a color VS task. In some trials, in which colored letters were displayed instead of colored VS items, participants had to report as many letters as possible (see Materials and methods and Figure 5). By manipulating the color of the letters, we were able to determine separately the effect of goal-directed and stimulus-driven salience on attentional allocation. Our working hypothesis was that if FEF or ANG is involved in salience representation, impeding their functions by means of TMS will modify the distribution of letter detection as a function of the salience of VS items, leaving the overall performance in the letter task unaltered.

EXPERIMENT 1

Materials and Methods

Participants

Eleven healthy participants (six women, mean age = 24 years) with normal or corrected-to-normal vision par-
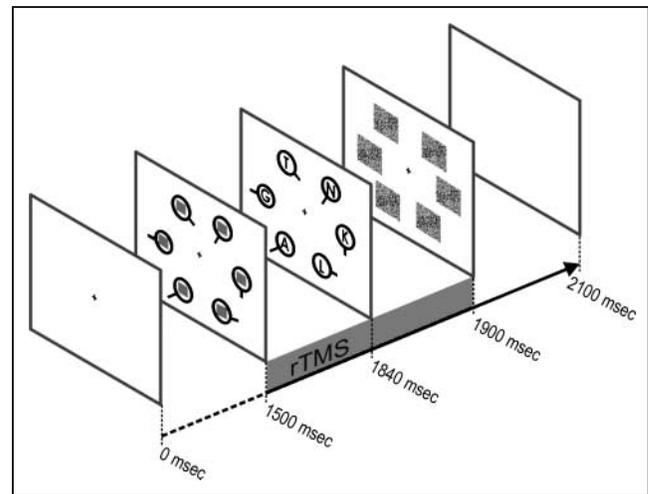
Figure 1. Experimental procedure of Experiment 1. After the display of the fixation point for 1500 msec, the items of the search were switched on. The target was the circle with a vertical line. After 340 msec (50 msec in control trials), letters were flashed for 60 msec inside each VS item, and all stimuli were then replaced by masks for 200 msec. rTMS was applied during the whole VS items display duration (five pulses at 10 Hz).

ticipated in the present study. One of them was excluded from the analyses because he performed a large number of saccades (>30% of trials) during the task. All experimental procedures were approved by the Ethics Committee of the Université catholique de Louvain, and participants gave their written informed consent. Monetary compensation was provided for their participation.

Task

Stimuli were presented on a 19-in. CRT monitor with a 100-Hz refresh rate. A personal computer running the Matlab 6.5 and the Cogent toolbox was used to control stimuli presentation and to trigger TMS. After the presentation of a central fixation point for 1500 msec, six VS items, that is, six circles appended with a bar oriented at 0°, 20°, 40°, 60°, 80°, or 100° either leftward or rightward from the vertical, were displayed at a 4° eccentricity from the screen center (Figure 1). The choice of this range of bar orientation (11 possible values) was based on the results of a pilot study and aimed to provide a robust effect of the item–target similarity (see Results section). The circle with a vertical bar was defined as the target and was displayed in 79% of trials. In the remaining 21% of the trials, the target was replaced by a distractor, randomly selected among the distractors described above. After 340 msec, a letter was flashed inside each VS item for 60 msec, followed by a 200-msec display of six random noise masks displayed at the same position as the VS items and randomly generated for each trial. Participants had first to report, as fast as possible, the presence or the absence of the target by pressing with the right index finger either the right or the left arrow key, respectively, and second, to report as many

letters as possible by typing them on the keyboard. Among the target-present trials, in 7% of trials, the letters were flashed 50 msec after VS items onset, and all stimuli were turned off and replaced by masks after 110 msec (control trials). This condition was added to make sure that participants did not perform the two subtasks sequentially instead of concurrently, performing the VS task first and then the letter detection task. Participants had no time constraint to type the detected letters, and they triggered the next trial by pressing the spacebar. Minimum intertrial interval was fixed at 10 sec.

Transcranial Magnetic Stimulation

Repetitive TMS (rTMS) was delivered with a Magstim Rapid system (Magstim Company, Wales, UK) through a 70-mm figure-of-eight induction coil, either over the right ANG or over the right FEF; the vertex (VX) was used as a control site. The rTMS train (10 Hz, five pulses, 400 msec) was synchronized with the onset of the VS display. The intensity of stimulation was fixed at 65% stimulator output, except for FEF stimulation in two participants, in whom TMS at such intensity elicited movements of the contralateral limb. For these two participants, the TMS intensity was reduced to 57% and 62%, respectively. For each participant, the coil position was precisely determined before each experiment by coregistering the stimulation sites onto individual anatomical MRI with a software developed in our laboratory (Noirhomme et al., 2004). Stimulation sites were localized in each participant according to anatomical landmarks, and stimulation coordinates were then normalized (Davare, Andres, Cosnard, Thonnard, & Olivier, 2006) according to the Montreal Neurological Institute atlas (see Figure 2). The ANG site was defined as the region directly adjacent to the dorsolateral projection of the superior temporal sulcus, and in the present study, the average coordinates of the stimulation site were 38.6 ± 1.8, −77.2 ± 2.7, and 40.6 ± 3.5 mm (mean ± SE; x, y, z, respectively), corresponding to coordinates previously used to target this area (Rushworth, Ellison, & Walsh, 2001). The coil was oriented in such a way that the induced current flowed into a lateromedial direction. The FEF stimulation site was localized at the intersection between superior frontal sulcus and precentral sulcus (Muggleton et al., 2003), at coordinates 36.8 ± 2.9, 2.2 ± 3.1, and 60.9 ± 1.9 mm, consistently with previous experiments (O'Shea, Muggleton, Cowey, & Walsh, 2006). The direction of the induced current was anterolateral. The VX was defined as a point midway between the inion and the nasion and was localized, on average, at the following coordinates: −0.5 ± 1.4, −15.6 ± 5.3, and 71 ± 2.8 mm. The induced current, when applied on the VX, flowed in a posteroanterior direction.

Each participant had to perform 12 blocks of 28 trials in one session. TMS was delivered in every trial. In each block, the stimulation site was pseudorandomly selected, with a total of four blocks per stimulation site (ANG, FEF, and VX).
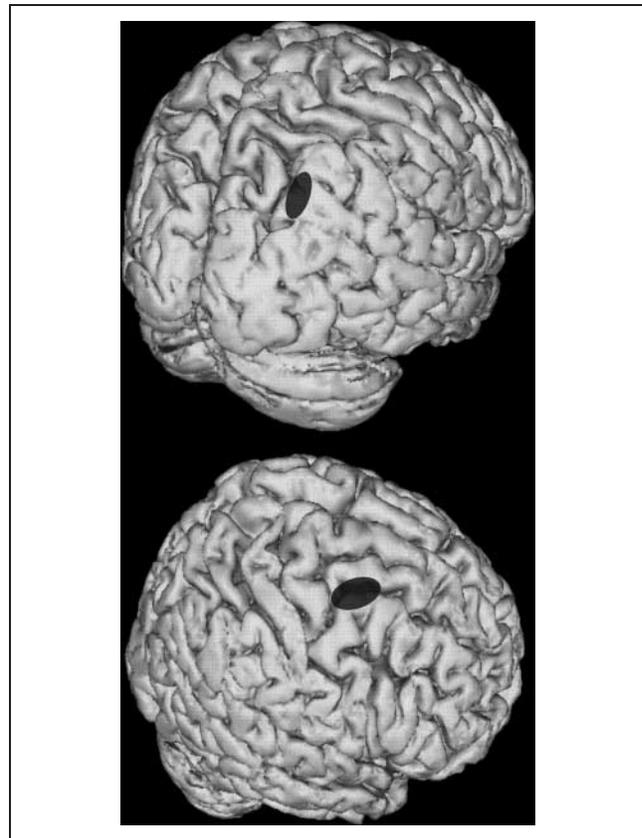
Figure 2. Coregistration of TMS sites. Mean location of stimulation sites over ANG (upper brain image) and FEF (lower brain image) after normalization into the MNI coordinate system. The ellipse surface indicates the 95% confidence interval. MRI scans were obtained in separate test sessions.

Data Acquisition and Analysis

Eye movements were monitored and recorded by means of an infrared camera (Thomas Recording, Giessen, Germany). An on-line saccade detection process permitted to give a feedback to the participants about their fixation performance: If a saccade was detected during a trial, a message was displayed on the screen for 1 sec at the end of the trial to inform the subject. Trials in which a saccade or a blink was detected during the stimuli presentation were discarded (mean ± SD = 12 ± 15 trials per session). Trials in which no target was present (21% of trials), and control trials (110 msec stimuli duration, 7% of trials) were not analyzed either. Statistical analyses were conducted on RTs, target, and letter report rates.

Inefficiency of the VS Task: Control Task A

The control task A was performed in 5 of the 11 participants; it consisted in reporting the presence or the absence of the target without paying attention to the letters flashed inside the VS items in displays containing either six or eight items. The visual items used this control task were identical to those used in the dual task (see above). This

task was performed on the same day, at the end of the main experiment and involved no TMS.

Stimulus-driven Effect of Horizontally and Vertically Oriented Items: Control Task B

In the control task B, eight different participants (four women, mean age = 25 years) had to perform a dual VS task comparable to that used in the main experiment but in which the orientation of the search items was irrelevant, the target being no longer defined by the orientation but by the length of its attached bar. The bar of the target was larger than that of the distractors for which the bar length was constant. The orientation of the bars, although irrelevant here, was different for each item and varied from 0° to 360° by steps of 15°. In that experiment, we analyzed the letter report rate as a function of the orientation of VS item bars. Each possible orientation was categorized based on its angle difference with respect to the horizontal, irrespective of the side (left or right) of the bar, yielding 13 different orientations.

Statistical Analysis

RT and target detection rate were compared across conditions by means of a two-way repeated measures (RM) ANOVA with Target Position ($n = 6$) and TMS Site (VX, FEF, or ANG) as independent variables. Letter report rate was studied by means of a four-way RM ANOVA, with the Orientation of the VS item in which the letter was displayed, the Letter Position on the screen, the Target Side (left or right hemifield) and the TMS Site (VX, FEF, or ANG) as independent variables. Post hoc comparisons are described in the Results section.

To achieve normality, an arc sine root transformation was systematically applied on percentages of detection (Zar, 1996).

Results

TMS Experiment: Behavioral Results

Overall, the VS target detection rate in the TMS experiment was $63 \pm 10\%$ (mean $\pm$ SD), and the false alarm rate was $35 \pm 11\%$. RT for target detection was 1311 ± 454 msec and, on average, participants reported 3.08 ± 0.79 letters per trial (mean $\pm$ SD). Only $47 \pm 7\%$ of these letters were correct, leading to a letter detection rate of 1.43 ± 0.46 letter per trial. This value was not significantly different in regular and control trials in which the letters were displayed only 50 msec after VS stimuli onset, one-way RM ANOVA, $F(1,9) = 3.11$, $p = .11$; this indicates clearly that participants did not systematically execute the subtasks in a given order, performing for instance the VS task before the letter detection task because if it was the case, the letter detection rate would have been reduced dramatically in these control trials. The control task A,

performed on six or eight VS items (see Materials and methods), proved that the VS task used in the present study was inefficient because the RT increased as a function of the number of VS items, one-way RM ANOVA, $F(1,4) = 16.93$, $p = .015$, slope $= 32 \pm 56$ msec/item. In the TMS experiment, we found that the letter report rate was influenced by the Orientation (RM ANOVA), $F(5,45) = 10.50$, $p < .0001$ (Figure 3), and the Letter Position, $F(5,45) = 3.90$, $p = .005$, in the display. The variation in the letter report rate as a function of the VS item orientation was nonlinear: Letters were detected more often when displayed in items with an orientation very similar (including the target itself) or very dissimilar to the target than in items with intermediate orientations. Letters were also better detected when displayed in VS items located along the horizontal meridian.

Similarly to the letter detection rate, the target detection performance was influenced by the Target Position, target detection rate, $F(5,45) = 2.48$, $p = .045$, RT, $F(5,45) = 4.45$, $p = .002$. Post hoc analyses (Tukey) showed a higher target detection rate and shorter RT when the target was located along the horizontal meridian (all $p < .05$). Surprisingly, interfering with ANG or FEF function had no effect on the VS performance, irrespective of the target location: target detection rate, $F(2,18) = 0.01$, $p = .989$; false alarm rate, $F(2,18) = 0.27$, $p = .765$; RT, $F(2,18) = 0.2$, $p = .847$; all Target Position $\times$ TMS Site interactions, $p > .05$).

TMS Experiment: Effect of TMS

Regarding the effect of TMS on the letter report rate, we found a strong interaction between TMS Site and Orientation of the VS items, $F(10,90) = 3.10$, $p = .002$ (see Figure 3A). The main effect of TMS and all other interactions
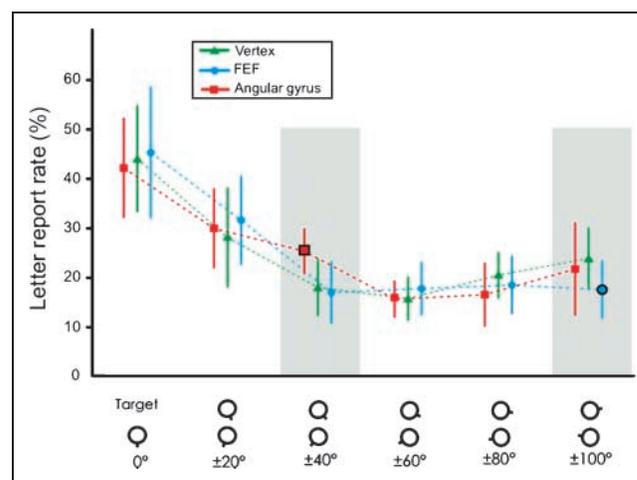

Figure 3. Effect of TMS on the letter report percentage as a function of orientation. Effect of TMS condition (color and shape code) and orientation of the search items (x-axis) on letter report percentage (y-axis). Error bars represent standard deviation from the mean. Significant differences between TMS site conditions are indicated by shaded areas and larger data points, outlined in black.

with TMS were not significant (all $p > .5$). More specifically, we failed to find a significant interaction between TMS Site and Target Side, $F(1,9) = 0.25$, $p = .78$, or Letter Position, $F(5,45) = 0.87$, $p = .57$. This absence of TMS Site $\times$ Letter Position interaction indicates that TMS applied over FEF or ANG did not change the influence of the letter position in the display on their detection rates. Post hoc analysis (comparison of the letter detection rate, for each orientation, as a function of the TMS Site condition, corrected for multiple comparisons) of the Orientation $\times$ TMS Site interaction indicated that the letters located inside VS items with a $\pm 40°$ orientation with respect to vertical were better detected following ANG than VX TMS ($p = .008$; see Figure 3), whereas those located inside VS items with a $\pm 100°$ orientation were less often detected when TMS was applied over the FEF than on the VX ($p = .044$; see Figure 3).

These interactions, although somewhat in agreement with our working hypothesis about the role of ANG and FEF in salience representation, are difficult to interpret without understanding the origin of the nonlinear relationship between the letter report rate and the orientation of VS items found in the control (VX) condition (see Figure 3). The results in the left part of this curve are easy to interpret and can be regarded as an effect of the goal-directed salience related to the item–target similarity (Zenon et al., 2008). In contrast, the reason why the letter report rate increased again in the right part of this curve for the VX condition is less evident, and we hypothesized that this effect could unveil a stimulus-driven factor of salience related to the horizontal orientation of the VS items. Indeed, vertical and horizontal orientations have been shown to be detected more easily (Foster & Ward, 1991; Rovamo, Virsu, Laurinen, & Hyvarinen, 1982), and orientations that can be clearly categorized, such as vertical or horizontal orientations, induce pop-out in VS tasks (Wolfe, Friedman-Hill, Stewart, & O'Connell, 1992).

Control Task B: Stimulus-driven Effect of Horizontally and Vertically Oriented Items

To test the hypothesis that horizontally oriented items attracted attention because of their high stimulus-driven salience value, we conducted a control experiment (control experiment B; see Materials and methods) with a dual VS task in which orientation of the search items was irrelevant. We confirmed that the letter report rate was indeed influenced by the Orientation of VS items, $F(12,84) = 1.98$, $p = .036$ (see Figure 4), although in this experiment this factor was irrelevant. To confirm our a priori hypothesis of a stimulus-driven effect of horizontality, we conducted a linear regression analysis of letter report probability as a function of orientation of the VS items for the four orientations close to the horizontal ($-30°$, $-15°$, $0°$, and $15°$ with respect to horizontal), corresponding to the orientations for which a stimulus driven of the horizontality was suspected in the main experiment. We found that the letter
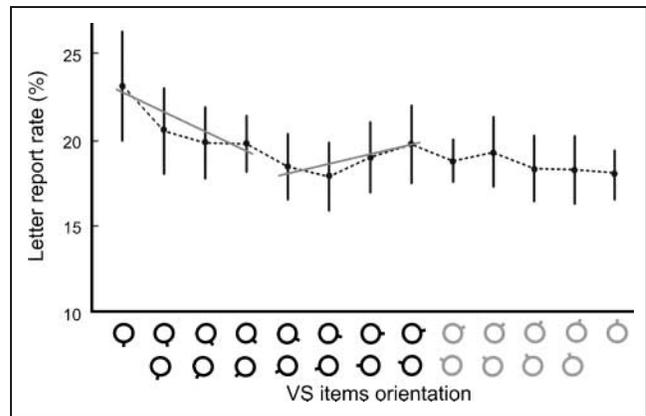
Figure 4. Effect of orientation on the letter report rate in the control task. Letter detection rate is represented as a function of the bar orientation. Error bars indicate standard deviation. The two gray lines indicate the two linear regressions performed to quantify the stimulus-driven effect of vertically and horizontally oriented items, as described in the text (see Materials and methods). The orientation values inside the range of orientations used in the main Experiment 1 are displayed in black on the x-axis; other orientation values are in gray.

report rate increased with horizontality ($R = .92, p < .0001$; see Figure 4). Consequently, we considered that this increase in letter detection performance for items orientation close to the horizontal in the TMS experiment unveiled a stimulus-driven effect. Because, in the TMS experiment, the target orientation was vertical, we also wanted to determine the possible stimulus-driven effect of vertically oriented stimuli. To do so, we performed a comparable regression analysis on the four orientations close to the vertical. Vertically oriented items also attracted attention in this control task ($R = .92, p < .0001$; see Figure 4). Therefore, the higher letter report rate found for vertically oriented items in the TMS experiment resulted probably from a combination of both stimulus-driven and goal-directed factors.

Discussion

In Experiment 1, we found that the orientation of VS items had both a goal-directed and a stimulus-driven influence on attentional allocation. Goal-directed influence depended on the resemblance of the VS items with the target, and indeed, letters flashed inside VS items with an orientation close to the vertical were detected with a higher probability because the target was vertically oriented. Unexpectedly, we also found that letters displayed in horizontally oriented VS items, although very different from the target, were reported with a higher probability. In control task B, we showed that even when the orientation was irrelevant to the task, participants still detected more often letters displayed in horizontally oriented items, demonstrating the stimulus-driven nature of this effect. In addition, letters displayed in vertically oriented items were also reported with a higher probability in this control task,

showing that the high report rate of letters displayed in vertically oriented VS items partly originated from a stimulus-driven influence.

Interestingly, we found that interfering with the normal function of ANG or FEF did not decrease the overall letter reporting rate or the VS performance but modified the influence of the orientation of VS items on the letter reporting probability. This effect was complex and seems to indicate that these two areas play an important role in salience representation. Indeed, we found that ANG virtual lesion improved the reporting rate of letters displayed in items showing a 40° difference with respect to the target, and because this effect specifically concerned letters displayed in items resembling the target, it could be regarded as evidence for the involvement of ANG in the representation of goal-directed salience. In contrast, TMS applied over FEF lowered the reporting rate of the letters displayed in the horizontally oriented items, suggesting an influence of FEF on stimulus-driven factors of attentional guidance.

To disentangle the contribution of ANG and FEF to the representation of the goal-directed and stimulus-driven salience, we conducted another experiment in which we investigated the effect of TMS on these two salience factors separately. Participants had to perform a color VS task but, at random, in some trials, letters were presented instead of the search items. The color of the letters was manipulated so that, except for one letter, their colors departed progressively from the color of the target in the VS task (goal-directed letter-reporting task); in another task, the letter color was adjusted so that it yielded different degrees of feature contrast (stimulus-driven letter-reporting task). Because, in the color VS task, participants were asked to focus on a given target color, we hypothesized that in the goal-directed letter-reporting task, letters with a color similar or close to that of the target would be more often reported, although participants had to report a maximum of letters irrespective of their color. This would unveil the effect of goal-directed guidance of attention by color. In the stimulus-driven letter reporting task, we predicted that letters with a high feature-contrast would be detected more often, providing a marker of the stimulus-driven guidance of attention. Therefore, by analyzing the letter reporting performance of the participants as a function of the color of the letters, we should be able to measure independently stimulus-driven and goal-directed effects on attentional allocation.

EXPERIMENT 2

Materials and Methods

Participants

Nine healthy participants (three women, mean age = 25 years) with normal or corrected-to-normal vision participated in Experiment 2. Subjects provided their informed consent before the experiment and were given monetary compensation for their participation in this study. The experimental procedure was approved by the Ethics Committee of the Université catholique de Louvain.

Task

The experimental setup used to control the stimuli presentation and to trigger TMS was the same as that used in Experiment 1. The task began with the presentation of a central colored circle for 2 sec (see Figure 5). The color of this circle was randomly selected among 10 possible isoluminant colors and was used to inform the participant about the color of the target he had to search for. Colors were represented by their hue, saturation, and brightness (hue saturation value [HSV] color space). Each color had the same saturation (65% of the maximum) and brightness (40% of the maximum) but differed in hue, with 36° differences between each successive color value. It is noteworthy that a constant difference in hue between two colors in the HSV color space does not necessarily imply a constant discrimination performance between these two colors, but this was not imperative in the present experiment. After the presentation of the colored circle, a central fixation point was displayed for 1 sec, and then one of three possible displays was presented with a probability of 0.33, each display corresponding to a different task:

1. *Orientation discrimination task*: Ten colored bars located on a virtual circle, at a 4° eccentricity, and at equal distance from each other, were displayed for 100 msec. Each bar had a different color—selected randomly among the same 10 possible colors as the central circle—and a different orientation, chosen randomly among 10 possible orientations ranging from 0° to 162° with respect to the vertical, by steps of 18°. The orientation of the target was always 18° away from the vertical, either clockwise or counterclockwise. After the presentation of the bars, 10 colored "X" letters, used as masks, were displayed at the same locations for 300 msec. The color of each "X" letter matched that of the bar previously displayed at the corresponding location.

2. *Goal-directed letter reporting task*: Ten colored letters were displayed for 100 msec on a virtual circle, at an eccentricity of 4° and at an equal distance from each other; each letter was different and had a different color. One of the letters, located at a random location, was defined as the target because it has the same color as the circle initially displayed at the trial onset. The color of the other letters became progressively more and more different from that of the target letter as their distances from the target letter increased (by step of 36° in hue value). Consequently, the color changed smoothly from one letter to the next one, avoiding abrupt color changes between neighboring letters. This ensured that no letter in the display had a higher feature contrast, and therefore a greater stimulus-driven salience than the others. This design yielded six different letter colors: the target color, the most different color with respect to the target, and four intermediate color values.
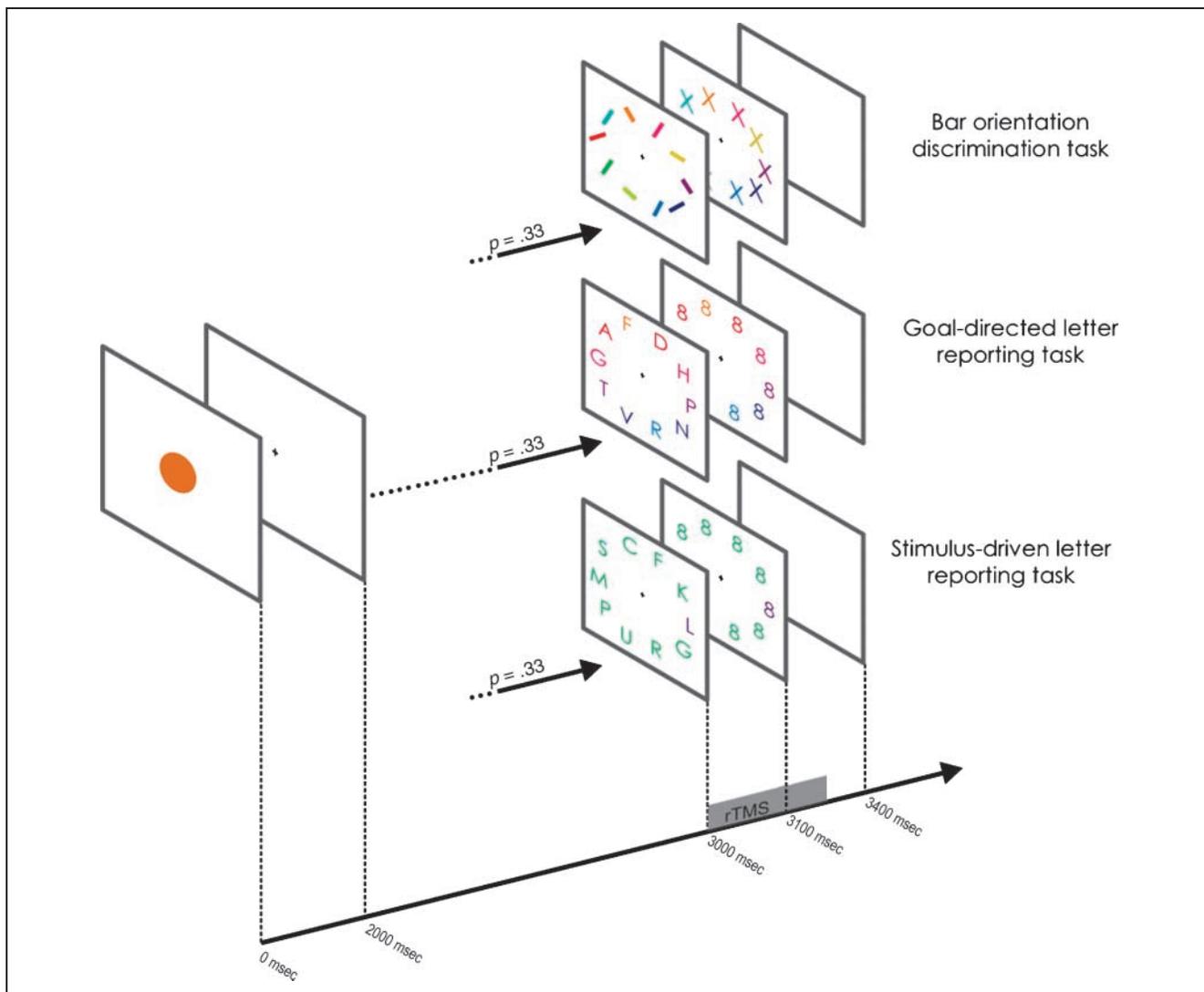
Figure 5. Experimental procedure of Experiment 2. After the display of the disk indicating the target color for 2 sec and the fixation point for 1000 msec, three different displays could appear for 100 msec, with equal probabilities, and were then replaced by masks for 300 msec. In the orientation discrimination task (upper row), 10 bars were displayed with different colors and participants were required to report the orientation of the bar with the target color. In the goal-directed letter reporting task (middle row), 10 different letters were displayed with a variable color difference with respect to the target color. In this case, participants had to report a maximum of letters. In the stimulus-driven letter reporting task (lower row), 10 different letters were displayed with two possible colors, both equally different to the target color. The number of letters in each of the two color groups was varied. Participants were asked to report a maximum of letters. In all conditions, rTMS was applied during a period of 240 msec, aligned on stimuli onset (five pulses at 16.66 Hz).

Each of the intermediate color values was attributed to two letters. Following the letter presentation, "8" figures of matching colors were displayed at each letter location, for 300 msec.

3. *Stimulus-driven letter reporting task*: Ten different letters were displayed on a virtual circle, at an eccentricity of 4°, and equally distant from each other. Only two colors were used in this task to characterize the letters; each color was equally distant to the target color defined at the beginning of the trial (i.e., at 120° from each other in the hue circle, and each at 120° from the target color). Therefore, in this task, no letter in the display had the same color as the target color defined by the initial central circle. One to three letters (each equally likely and pseudo-

randomly interleaved) were of one color, and 9 to 7 letters were of the other color. For each "target" color, the same pair of colors was always used, and the color used for the smallest group of letters was selected at random. After the letter presentation, "8" figures with matching colors were displayed at each letter location, for 300 msec.

The task differed according to the stimuli displayed, and participants were unable to predict the task they had to perform in the next trial. When the bars were displayed, the task consisted in determining the orientation of the bar matching the target color, as indicated by the colored circle initially displayed at the onset of the trial. Participants had to press either the left or the right arrow key

to indicate, respectively, whether the target bar was rotated counterclockwise or clockwise with respect to the vertical. Participants were encouraged to respond as quickly and as accurately as possible, and they received an auditory feedback when their responses were incorrect. When the letters were displayed, participants had to report as many letters as possible, with no time constraint. In this case, no feedback was given to the participants.

Transcranial Magnetic Stimulation

The stimulation conditions were the same as in Experiment 1, except that the frequency of the stimulation pulses was higher, the rTMS train consisting of five pulses delivered with an interpulse interval of 60 msec (16.66 Hz). This parameter was modified because the stimuli were displayed only for 100 msec; hence, it was not appropriate to have an rTMS train lasting for 400 msec. The first pulse was synchronized with the onset of the stimulus display. Stimulation was delivered at 65% of the stimulator output, except for three participants, in whom TMS at this intensity applied over FEF elicited either blinks or movements in the contralateral limb. TMS intensity was therefore reduced to 55% in two of these participants and to 58% in the third one. Stimulation sites were localized using the same procedure as that used in Experiment 1. In this experiment, the ANG, the FEF, and the VX sites were localized, respectively, at 41.0 ± 1.0, −79.7 ± 2.2, and 32.8 ± 3.2 mm; 38.1 ± 2.6, 1.1 ± 2.1, and 61.8 ± 2.5 mm; and −2.9 ± 1.2, −10.5 ± 4.2, and 74.8 ± 1.2 mm (mean ± *SE*; *x, y, z*). Participants performed 12 blocks of 36 trials each, leading to a total of 432 trials.

Results

Overall, the percentage of correct responses in the bar orientation discrimination task was 60 ± 10% (mean ± *SD*) and, on average, RTs were 1040 ± 194 msec. Separate RM ANOVAs were performed to determine the effect of the bar Position and the effect of the bar Color on both the orientation discrimination rate and the RT. In these ANOVAs, the independent variables were the Position of the bar in the display ($n = 10$) and the TMS Site ($n = 3$). This analysis did not yield significant effects; percentage of correct response: main effect of Position, $F(9,72) = 0.98$, $p = .47$, TMS Site, $F(2,16) = 0.22$, $p = .80$, Position × TMS Site interaction, $F(18,144) = 0.94$, $p = .53$; RT: main effect of Position, $F(9,72) = 1.68$, $p = .11$, TMS Site, $F(2,16) = 0.84$, $p = .45$, Position × TMS Site interaction, $F(18,144) = 0.92$, $p = .55$. Similarly, the color of the bar ($n = 10$) did not affect either the orientation discrimination rate or the RT, irrespective of the TMS site location; main effect of Color, $F(9,72) = 1.40$, $p = .21$, TMS Site, $F(2,16) = 0.44$, $p = .65$, Position × TMS Site interaction, $F(18,144) = 0.97$, $p = .50$; RT: main effect of Color, $F(9,72) = 1.62$,

$p = .13$, TMS Site, $F(2,16) = 0.93$, $p = .41$, Position × TMS Site interaction, $F(18,144) = 0.93$, $p = .54$.

The letter report rate in the two letter-reporting tasks was found to depend on the color (HSV value) of the displayed letter, one-way RM ANOVA, $F(9,82) = 10.85$, $p < .0001$, the performance being inferior for colors in the yellow-orange range than for the other colors (Tukey post hoc comparisons, all $p < .05$). However, because the target color was pseudorandomly selected among the 10 possible colors, the influence of the color on the letter detection performance does not affect the validity of the following analyses.

Results of the Goal-directed Letter Reporting Task

Concerning the goal-directed letter reporting task, we conducted a three-way RM ANOVA with Position of the letter in the display ($n = 10$), TMS Site, and Color ($n = 6$, 1 corresponding to the target color and six to the most different color) as independent variables. The overall letter reporting performance was significantly influenced by Color and Position, main effect of Color, $F(5,40) = 8.02$, $p < .0001$, main effect of Position, $F(9,72) = 5.04$, $p < .0001$, but not by TMS, main effect of TMS Site, $F(2,16) = 0.49$, $p = .62$. Critically, the only significant interaction we found was between Color and TMS Site, $F(10,80) = 2.82$, $p = .005$ (see Figure 6A). Post hoc analysis (Tukey) of the Position effect showed that letters located along the horizontal meridian were reported more often, with an additional bias for the right hemifield. The color effect consisted in a higher report rate of letters with a color similar or close to the target color (see Figure 6A, in which this effect was decomposed as a function of the TMS Site). The Color × TMS Site interaction showed that whereas the color effect in the VX control condition was small but significant (fifth color level significantly different than the first and second color levels, all $p < .05$), the influence of color on letter report probability increased when TMS was applied over ANG and FEF. In particular, the first and the fourth color levels were different between the FEF and the VX stimulation conditions, and the first and the sixth color levels differed between the ANG and the VX conditions (post hoc comparisons between stimulation sites, for each color value, corrected for multiple comparisons, all $p < .05$).

Results of the Stimulus-driven Letter Reporting Task

For the analysis of the stimulus-driven letter reporting task, we conducted a similar three-way RM ANOVA with position of the letter in the display ($n = 10$), TMS Site, and the number of letters in the Color Group ($n = 8$, from 1 to 9, excluding 5, each value corresponding to the number of letters of the same color) as independent variables. The overall letter reporting performance was significantly influenced by Color Group and Position, main effect of Color Group, $F(7,56) = 6.10$, $p < .0001$,
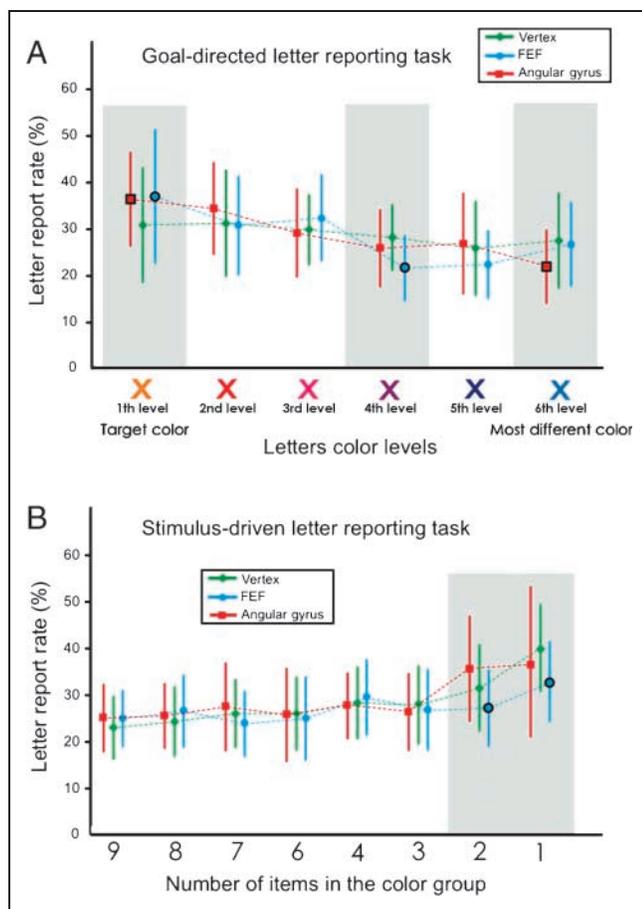
Figure 6. Results of Experiment 2. Effect of TMS condition (color and shape code) and color (*x*-axis) on letter report percentage (*y*-axis) in the goal-directed letter reporting task (A) and the stimulus-driven letter reporting task (B). Error bars represent standard deviation. Significant differences between TMS site conditions are indicated by shaded areas and larger data points, outlined in black.

main effect of Position, $F(9,72) = 9.39$, $p < .0001$, and not by TMS, main effect of TMS Site, $F(2,16) = 0.27$, $p = .77$. Here also, the only significant interaction we found was between Color Group and TMS Site, $F(10,80) = 3.03$, $p = .001$ (see Figure 6B). Post hoc analyses showed that the Position effect was the same as in the goal-directed letter reporting task, with a preference for letters located on the horizontal meridian and a bias for the right hemifield. The Color Group effect consisted in a higher detection rate of letters with a color that was unique in the display or shared by only one other letter (see Figure 6B). The Color Group × TMS Site interaction showed that TMS applied over FEF impeded significantly this effect by decreasing the letter reporting rate in the color group containing one or two letters of the same color (all $p < .05$).

Discussion

The tasks used in Experiment 2 allowed us to determine separately the effects of stimulus-driven and goal-directed

factors on attentional allocation. The bar orientation discrimination task was used to force participants to focus on the target color, whereas the two letter-reporting tasks were used to measure independently the stimulus-driven and goal-directed effects of color on the letter detection rate. In the goal-directed letter reporting task, we found that participants detected more often letters with a color close to the target color, providing us with a measure of the goal-directed salience. In the stimulus-driven letter reporting task, we found that the letter reporting rate was higher for letters with a color that was unique in the display or shared by only one other letter. This so-called "feature-ratio" effect is independent of the target color; hence, it is a stimulus-driven factor of attentional guidance.

As in Experiment 1, in which TMS failed to influence the overall performance in the VS task, in Experiment 2 interfering with the ANG or the FEF function had no effect on the orientation discrimination rate and the RT in the bar orientation task. In contrast, TMS applied over ANG affected the letter report probability in the goal-directed task only, increasing the report rate only for letters with the same color as the target and decreasing this rate for letters with the most different color from the target. Additionally, interfering with FEF function affected the letter report rate in both the stimulus-driven and the goal-directed tasks. In the stimulus-driven letter reporting task, TMS applied over FEF hampered the stimulus-driven effect of color in the same way as in Experiment 1 in which it decreased the stimulus-driven effect of horizontality. Moreover, we found that FEF TMS altered the letter report rate in the goal-directed letter reporting task because interfering with FEF increased the reporting rate for letters with the target color and decreased it for letters with the fourth color level corresponding to a 144° hue difference from the target color. As in Experiment 1, we failed to find any effect of ANG or FEF interference on the overall letter report probability.

It is noteworthy that in this experiment, in contrast to Experiment 1, we modified the salience of the letters by changing their color. Consequently, it cannot be excluded that the effects we measured in the goal-directed letter-reporting task were, at least partly, related to feature-based attention or other type of color priming phenomenon, in addition to the guidance of spatial attention by goal-directed factors.

GENERAL DISCUSSION

Both the parietal and the frontal cortex are usually regarded as critically involved in the control of spatial attention (Schall, 2004; Corbetta & Shulman, 2002; Goldberg, Bisley, Powell, Gottlieb, & Kusunoki, 2002), and more specifically, it has been suggested that these two brain regions could house a salience map that prioritizes the different objects present in the visual field (Thompson & Bichot, 2005; Kusunoki, Gottlieb, & Goldberg, 2000; Gottlieb et al., 1998). According to this view, the neural activity in those

brain regions should be proportional to the conspicuity and/or the relevance of visual objects for the task at hand, and these areas should be involved in guiding attention and gaze shifts. In agreement with this latter hypothesis, our results show that interfering with the normal function of ANG or FEF hampered the influence of salience on attentional allocation without affecting the global letter report rate. In addition, the present study gives further insight into the specific role of ANG and FEF in salience representation. Indeed, the tasks we used allowed us to dissociate two different factors of salience: (a) the goal-directed effect of the item–target similarity on letter report rate, and (b) the stimulus-driven effects of the horizontal orientation and of the feature-ratio effects. Interestingly, we found that TMS over ANG affected distinctly the influence of item–target similarity, whereas TMS over FEF seemed to affect both stimulus-driven and goal-directed factors of salience.

However, the present results are somewhat difficult to interpret because TMS applied over the same area induced contrasting effects, that is, either a decrease or an increase in the letter report performance, and these effects cannot simply be regarded as a worsening or an improvement of the effect of salience factors on attentional allocation. The finding that TMS induces opposite effects on a given task is not novel. Several TMS studies have already shown that stimulation of one area can yield either disruptive or facilitative effects depending on the task at hand (Romei, Murray, Merabet, & Thut, 2007; Sack et al., 2007; Grosbras & Paus, 2002; Walsh, Ellison, Battelli, & Cowey, 1998), the baseline level of cortical excitability (Silvanto, Cattaneo, Battelli, & Pascual-Leone, 2008; Silvanto, Muggleton, Cowey, & Walsh, 2007), the hemifield in which the stimulus was displayed (Fecteau, Pascual-Leone, & Theoret, 2006; Thut, Nietzel, & Pascual-Leone, 2005), or the parameters of the stimulation (Houdayer et al., 2008; Jung, Shin, Jeong, & Shin, 2008; Fierro et al., 2005). In the present study, several factors may have influenced the facilitative versus disruptive effects of TMS on the different tasks we investigated. First, TMS may alter the interactions between the two hemispheres; for instance, TMS could have led to a suppression of the inhibition the stimulated area normally exerts on the homologous region of the opposite hemisphere, inducing an increased activity or excitability of the latter. If this holds true, TMS applied over right ANG would have led to an increased activity/excitability of left ANG, which could be involved in the selection of low salient stimuli (Mevorach et al., 2008). Accordingly, the enhanced detection of items with low goal-directed salience we found in Experiment 1 could result from a disinhibition of the left ANG consequent to an interference of right ANG induced by TMS. However, this hypothesis fails to explain the results we observed in Experiment 2, in which letters with the lowest goal-directed salience value were less often detected following right ANG TMS. A second possible explanation for these contrasting effects of TMS is that a winner-take-all process of selection is imple-

mented in the salience map, leading to the singling out of the most salient location (Bisley & Goldberg, 2003; Koch & Ullman, 1985). Applying TMS over a cortical area in which such a process takes place can lead to very complex results both by changing the level of activity in different map points and by altering the mutual interactions between them. Finally, it could be assumed that although each pulse of the TMS train induces a facilitation of cortical cells located in the stimulated area, repetitive stimulations leads to a longer lasting inhibition of these cells (Allen, Pasley, Duong, & Freeman, 2007), leading therefore to complex effects of TMS, depending on the balance between transient facilitation and more prolonged inhibition. Hence, the consequences of rTMS on behavior may vary dramatically depending on the exact timing of each pulse with respect to the time course of the process ongoing in the stimulated area.

The absence of effects of TMS applied over ANG and FEF on VS performance in Experiments 1 and 2 contrasts strikingly with previous works (Kalla, Muggleton, Juan, Cowey, & Walsh, 2008; Muggleton et al., 2003, 2008; O'Shea, Muggleton, Cowey, & Walsh, 2004; Walsh, Ashbridge, & Cowey, 1998; Ashbridge et al., 1997). As far as ANG is concerned, previous studies have repeatedly found that interfering with the function of this area increases RT and alters the performance in VS tasks. Possible explanations for a lack of effect of ANG interference on VS performance in the present study are that participants were highly trained and performed feature VS tasks. In contrast, in their study, Walsh et al. (1999) showed that single pulse TMS applied over right ANG affected RT in conjunction VS and only when participants had little or no experience with the task, and most previous work found that TMS affects conjunction, but not feature, VS (Muggleton et al., 2008). As far as the consequences of FEF virtual lesions are concerned, previous studies have reported an increase in false alarm rate in conjunction VS (O'Shea et al., 2004; Muggleton et al., 2003). Again, because in the present study we used a feature and not a conjunction VS task, this could explain the discrepancy with previous results. In addition, in Experiment 1, the number of target-absent trials was too low to draw an unambiguous conclusion about the absence of effects of FEF interference on false alarm rate. In Experiment 2, the target was always present and participants had to perform a two-alternative forced-choice task, in which no false alarm can occur. Consistently with the hypothesis that ANG and FEF are involved in the computation of a salience map, the effects of TMS found on VS tasks in previous studies can be interpreted as a consequence of the disruption of salience computation and the finding that interfering with ANG and FEF only affects conjunction VS tasks, and mainly when they are novel, would suggest that these VS tasks rely more on attentional guidance than other types of VS tasks.

Beyond studies using VS, a large body of evidence supports the role of ANG and FEF in attentional processes. The

implication of ANG in non-VS attentional tasks has received multiple converging evidence in TMS (Chambers & Mattingley, 2005) and fMRI studies (Donner et al., 2002; Yantis et al., 2002; Culham, Cavanagh, & Kanwisher, 2001). In monkeys, Area 7a, the probable homologue of ANG (Rushworth, Behrens, & Johansen-Berg, 2006; Van Essen et al., 2001), contains neurons whose activity depends on the presence of a salient stimulus in their receptive fields (Constantinidis & Steinmetz, 2005), suggesting that Area 7a contributes to salience representation. This hypothesis has been confirmed and extended in the present study by showing a specific role for ANG in goal-directed salience representation in humans. Evidence for the FEF implication in attentional processes also comes from many studies using different approaches such as single cell recordings (Thompson et al., 2005; Schall, 2004), microstimulation (Moore & Armstrong, 2003), transient inactivation (Wardak, Ibos, Duhamel, & Olivier, 2006), functional neuroimaging (Simon et al., 2004), neuropsychology (Mesulam, 1999), and TMS (Silvanto, Lavie, & Walsh, 2006; O'Shea et al., 2004; Muggleton et al., 2003; Grosbras & Paus, 2002). Some of these studies have already suggested a role of FEF in controlling shifts of attention dependant on stimulus-driven salience (Lavie & De Fockert, 2006; Wardak et al., 2006; Grosbras & Paus, 2002), and some have suggested its implication in goal-directed factors (Smith, Jackson, & Rorden, 2005) whereas others have reported both (Kincade, Abrams, Astafiev, Shulman, & Corbetta, 2005). The present results are in line with this latter hypothesis, providing support for the contribution of FEF to both stimulus-driven and goal-directed salience computation.

In conclusion, we propose that both ANG and FEF are involved in the computation of visual salience. Whether they are also involved in the implementation of the attentional shifts, that is, in the generation of the attentional signal that enhances sensory processing at selected spatial locations (Moore & Armstrong, 2003; Pessoa, Kastner, & Ungerleider, 2003), remains an open question. The finding that the disruption of their normal functions by TMS led to a deficit in attentional allocation that depends on the salience level, although it had no effect on the global letter report, suggests that the capacity to shift attention was preserved and that only the processes involved in the selection of the attentional target were disrupted. The attentional signal per se might originate from other brain structures such as the superior colliculus (Carello & Krauzlis, 2004; Cavanaugh & Wurtz, 2004; Kustov & Robinson, 1996). Alternatively, attentional modulation might arise directly from feedback signals coming from ANG and FEF salience maps (Hamker, 2004), requiring no additional structures. In this case, TMS, by adding noise in the system (Pascual-Leone, Walsh, & Rothwell, 2000), would perturb the selectivity of the modulation signal but would not prevent the generation of attentional shifts. This would result in a reduced effect of salience on attentional allocation without any decrease in global detection performance, as reported in the present study.

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