The role of frontal pursuit area in interaction between smooth pursuit eye movements and attention: A TMS study

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Close coupling between attention and smooth pursuit eye movements has been widely established and frontal eye field (FEF) is a "hub" region for attention and eye movements. Frontal pursuit area (FPA), a subregion of the FEF, is part of neural circuit for the pursuit, here, we directly checked the role of the FPA in the interaction between the pursuit and attention. To do it, we applied a dual-task paradigm where an attention demanding task was integrated into the pursuit target and interrupted the FPA using transcranial magnetic stimulation (TMS). In the study, participants were required to pursue a moving circle with a letter inside, which changed to another one every 100 ms and report whether "H" (low attentional load) or one of "H," "S," or "L" (high attentional load) appeared during the trial. As expected, increasing the attentional load decreased accuracy of the letter detection. Importantly, the FPA TMS had no effect on both the pursuit and letter detection tasks in the low load condition, whereas it reduced 200 to 320 ms gain, but tended to increase the letter detection accuracy in the high load condition. Moreover, individual's FPA TMS effect on pursuit gain was significantly correlated with that on letter detection accuracy. Presumably, the pursuit gain control by the FPA was compensated by attention in low load condition, and the FPA may flexibly allocate attentional resources between the pursuit and letter detection task in high load condition. Altogether, it seems that the FPA has a control over attentional allocation between tasks.

Introduction

Smooth pursuit eye movements refer to ocular tracking of moving targets, maintaining the image of targets on the fovea. Many studies demonstrated a close relationship between the pursuit and attention (e.g., Acker & Toone, 1978; Van Gelder et al., 1995; Kathmann et al., 1999; Hutton & Tegally, 2005; Kerzel et al., 2009; Stubbs et al., 2018). Attention is allocated around the pursuit target (Lovejoy et al., 2009; Watamaniuk & Heinen, 2015) and the pursuit shares attention with a wide range of attention demanding

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tasks, including auditory and visual discrimination, saccades, detection, and so on (Hutton & Tegally, 2005; Kerzel et al., 2009; Jin et al., 2013). These studies checked the relationship between attention and the pursuit by manipulating attention using dual-task design. A group of studies divided attention from the pursuit by performing a cognitive or perceptual task unrelated to the pursuit target. Using this type of design, studies found the pursuit was impaired by the additional attention tasks (Acker & Toone, 1978; Hutton & Tegally, 2005; Kerzel et al., 2009). Relatively few studies used another type of dual-task design, where the attention task was integrated into the pursuit target. Related studies consistently found that enhanced attention by the additional task improved overall performance of the pursuit (Clementz et al., 1990; Stubbs et al., 2018). Thus, the present study applied this type of dual-task design to investigate neural bases of the interaction between attention and smooth pursuit eye movements.

Widely, it has been established that the smooth pursuit eye movements generation network includes cortical and subcortical brain regions (Krauzlis, 2004; Leigh & Zee, 2006). The frontal pursuit area is part of the smooth pursuit generation network and it is proposed to be responsible for dynamic gain control (Nuding et al., 2008). Human neuroimaging studies showed activations of the pursuit-related region in the frontal eye field (FEF) during the pursuit (Petit et al., 1997; Berman et al., 1999; Petit & Haxby, 1999; Rosano et al., 2002; Nagel et al., 2006) and BOLD response in the left FEF was negatively correlated with the eye velocity gain during the pursuit (Nagel et al., 2006). Evidence of the role of the frontal pursuit area (FPA) in the pursuit also came from transcranial magnetic stimulation (TMS) studies (Gagnon et al., 2006; Drew & Van Donkelaar, 2007; Nuding et al., 2009). TMS over the FPA reduced overall velocity gain and reduced the slope of the eye velocity gain increase when the pursuit target increased velocity (Nuding et al., 2009). When the pursuit target moved in a sinusoidal trajectory, the FPA TMS increased the eye velocity in the new direction if the TMS was delivered immediately before the target reversed direction, but decreased eye velocity if the TMS was delivered when the target began to decrease the velocity, suggesting a role of the FPA in the pursuit gain control to predictive motion signals (Gagnon et al., 2006). TMS to the FPA given after the motion onset delayed contraversive pursuit more than ipsiversive pursuit and this difference was bigger with the unpredictable pursuit than the predictable one (Drew & Van Donkelaar, 2007). In addition to a critical role in the pursuit, the FEF is an important node of the frontoparietal network, which plays a crucial role in covert orienting of attention (Corbetta et al., 1998; Corbetta & Shulman, 2002, 2011 for reviews). As shown before, behavioral studies found a strong coupling between the pursuit and attention (e.g. Acker & Toone, 1978; Hutton & Tegally, 2005; Kerzel et al., 2009; Lovejoy et al., 2009; Watamaniuk & Heinen, 2015; Stubbs et al., 2018). Combining significant roles of the FEF in both attention and smooth pursuit generation, the FPA may be a promising candidate for the interaction between the pursuit and attention. However, to our knowledge, no direct evidence of the role of the FPA underlying coupling between the pursuit eye movements and attention has been found.

Thus, we set out to examine the role of the FPA in attention and smooth pursuit eye movements using TMS. A dual-task paradigm was designed for investigating the interaction between the pursuit and attention. In the paradigm, participants were required to pursue a moving object and perform a letter detection task at the same time. The letter detection task was endowed on the pursuit target and varied in attentional demands in two levels, low and high load. In addition, continuous theta burst stimulation (cTBS) was applied over the right FPA (rFPA) to suppress neuronal activities (Huang et al., 2005; Chung et al., 2016). The right primary motor cortex (rM1) was stimulated as a control. Here, we mainly evaluated the eye velocity gain as pursuit measure and the accuracy of letter detection task as behavioral measures of attention. We focused on whether and how the pursuit gain and the letter detection rate were modulated by the right FPA TMS. We showed the TMS over the FPA modulated the pursuit gain and letter detection rate, especially if the detection task had a high load, not a low load, suggesting a capacity limit mechanism in attentional resources. When available resources were insufficient for both tasks, the suppression of the FPA modulated either the pursuit or the letter detection performance. In summary, the right FPA is responsible for pursuit and attention and it distributes resources between tasks.

Methods

Participants

Sixteen right-handed students (7 men) from the University of Electronic Science and Technology of China (UESTC), with a mean age of 22.4 years (SD = 1.9), participated in the study. All participants had normal vision and none of them had a history of neurological diseases. The current study followed the published guidelines of the use of TMS in clinical practice and research and the study was approved by the Functional Magnetic Resonance Imaging (fMRI) Research Center in the UESTC and the Human Body Protection Board. All participants were naïve to the

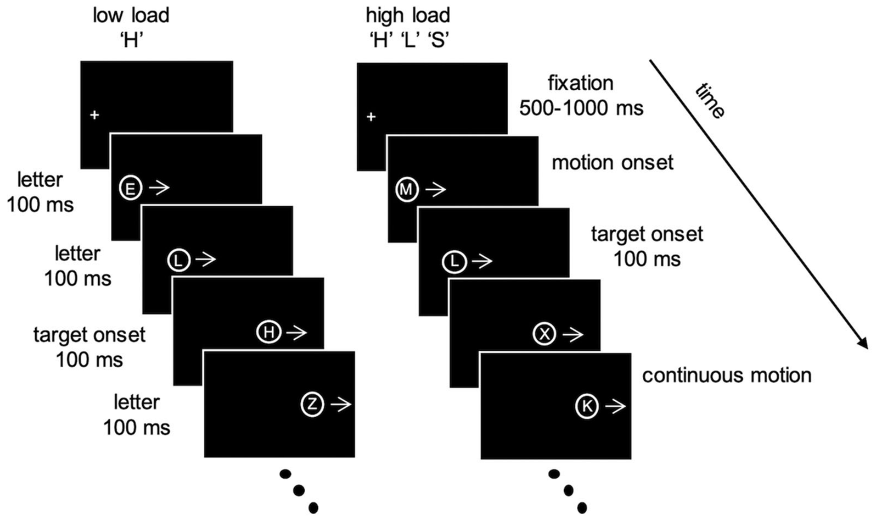

Figure 1. Schematic trial procedure. Fixation cross appeared at the left or right part of the display for 500 to 1000 ms (here shows the fixation cross appeared in the left). Observers fixated the fixation cross, and then pursued it as the stimulus moved towards the display center at 10.71 degree/second for 1.5 second. Letter in the circle changed every 100 ms and the target letter appeared 400 to 800 ms after motion onset. The target letter was either "H" (low load condition) or one of three letters ("H," "L," and "S", high load condition). Only half of trials had the target letter appeared. Observers were instructed to pursue the stimuli until the end of trial and judge whether a target letter was presented.

aim of the study and signed written informed consent and were compensated for the participation.

Apparatus

Visual stimuli were generated using MATLAB (The Mathworks, Inc., Natick, MA, USA) using PsychToolbox-3 (Brainard, 1997; Pelli, 1997; Kleiner, 2007) and presented on a display with 1024 × 768 pixels resolution at the refresh rate of 60 Hz. Both horizontal and vertical eye movements were recorded by the EyeLink 1000 system (SR Research Ltd., Ottawa, Ontario, Canada) at a sampling rate of 2000 Hz. Viewing was binocular, but only the right eye positions were recorded. A 2T Magstim 200 delivered through a figure 8 coil was used to deliver TMS and the stimulation site was positioned using BrainSight Stereotaxic Neuronavigator (Rogue Research, Montreal, Canada), equipped with a Polaris Vicra position sensor system. The study was conducted in a dim, quiet, and enclosed room and the participants sat at a constant viewing distance of 55 cm from the display with the help of a chin and forehead rest.

Stimuli and trial procedure

The present study applied a dual-task paradigm with a letter detection task endowed on the pursuit target. The pursuit target was composed of a circle (1 degree in diameter) and an upper-case letter inside it (see Figure 1). Only letters without any hole were picked as stimuli to avoid any potential effect caused by the hole effect ("C," "E," "F," "G," "H," "I," "J," "K," "L," "M," "N," "S," "T," "V," "X," "U," "W," "Y," and "Z"). Among these, "H," "L," and "S" served as the target stimuli of the letter detection task and they never served as distractors. All stimuli were drawn in white (RGB [255 255 255]) and were displayed on a black background (RGB [0 0 0]).

Each trial (see Figure 1) started with a 500 to 1000 ms of fixation duration with a fixation cross (0.43 degree in length), which was presented at the left or right (8.04 degrees from the display center) part of the display. After the fixation, the pursuit target appeared at the fixation location and began to move toward the display center. The pursuit target moved at constant velocity of 10.71 degrees/second for 1.5 seconds and disappeared after the movement. Letters in the circle changed to another one every 100 ms and the target letter appeared 400 to 800 ms since the stimuli movement onset, enabling all targets to appear during the steady-state of the pursuit. Only half of the trials had a detection target that appeared and the participants were required to judge whether a target letter appeared during the trial and responded by clicking the mouse button at the end of each trial (left click for Yes and right click for No). Attentional load of the detection task was manipulated by changing the number of potential targets, one ("H"; low load) or three ("H," "L," and "S"; high load) targets. Low

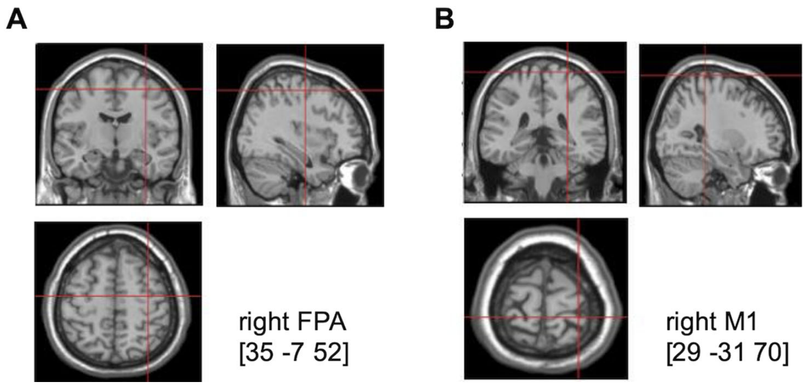

Figure 2. TMS stimulation sites. (**A**) The location of the right FPA (rFPA), [35 -7 52] in Talairach coordinate. (**B**). The location of the right primary cortex (rM1), [29 -31 70] in Talairach coordinate. The position was verified using individual MRI scan co-registered to their head landmarks using BrainSight software.

and high load task conditions were separated using a blocked design and potential targets never served as distractors to avoid confusion (i.e. "S" and "L" were never presented as distractors in the low load block). Each block contained 64 trials and every participant ran one block of low and high load block before and after the TMS over two target brain sites (right FEF and right M1; see Figure 2). Hence, every participant performed eight blocks in total ($8 \times 64 = 512$ trials). Between blocks, the participants took a several-minutes break and the order of TMS stimulation over the right FPA and right M1 were counterbalanced across the participants.

TMS protocol and stimulation sites

A Magstim super rapid stimulator equipped with a prevalent 70-mm figure-8 coil was used to deliver TMS pulses (Magstim Company Limited, Whiteland, UK). Offline cTBS at 29% of the stimulator maximum output was administered. This intensity was much lower than the motor threshold, which was usually around approximately 60 to 70% of the maximum output for our participants. Here, every train of cTBS consisted of 3 pulses every 200 ms at 50 Hz, and 200 bursts with a total of 600 pulses were delivered to the right FPA ([35 -7 52] in Talairach coordinate; Gagnon et al., 2006; Nuding et al., 2009) and the primary motor cortex (M1) ([29 -31 70] in Talairach coordinate) as a control site, which corresponds to the left elbow joint movements (Gao et al., 2006). In order localize the stimulation site, individuals' high-resolution T1-weighted magnetic resonance imaging (MRI) was obtained using a 3.0 T GE Sigma scanner (General Electric, Milwaukee, WI, USA). The scanner parameters were set as TR = 5.96 ms, TE = 1.96 ms, FA = 9 degrees, FOV = 256×256 mm^2, voxel size = $1 \times 1 \times 1$ mm^3, 176 slices, and 1 mm thickness with no gap. Landmarks on the participants' head were coregistered to individual MRI anatomic scans using a frameless stereotaxy system (BrainSight Frameless; Rogue Research). BrainSight was used to track the position of the TMS coil throughout the stimulation period, ensuring that it remained on the target TMS stimulation location. As mentioned before, the order of stimulation sites was counterbalanced across the subjects. Between the TMS over the two stimulation sites, there were at least 3 hours to avoid potential interference of the TMS stimulation over the first brain area, which is much longer than the duration of the cTBS effect (Huang et al., 2005; Chung et al., 2016). The TMS session was performed according to the published safety guidelines (Wassermann et al., 1996; Rossi et al., 2009).

Data analysis

We analyzed eye movements' data offline. Horizontal and vertical eye positions were collected and processed through the Butterworth Filter frequency of 50 Hz to obtain the eye velocity. Saccade detection used velocity threshold of 30 deg/s. Trials with blink during the stimuli movement were excluded from the analysis. According to these criteria, 98.7% of trials on average were retained for further analysis for each participant.

First, we analyzed the accuracy of the letter detection task. Then, for the pursuit data analysis, we determined pursuit latency for each participant in each condition using the median velocity traces. We first aligned velocity traces to stimuli movement onset and computed the median traces of each condition for each subject. Considering anticipatory pursuit, we picked [-50 50] ms time interval relative to the movement onset as the baseline time interval. Later, 80 ms regression lines started from 80 ms to 300 ms were fitted to median velocity trace and the best fitting regression line was selected from all regression lines with a slope between

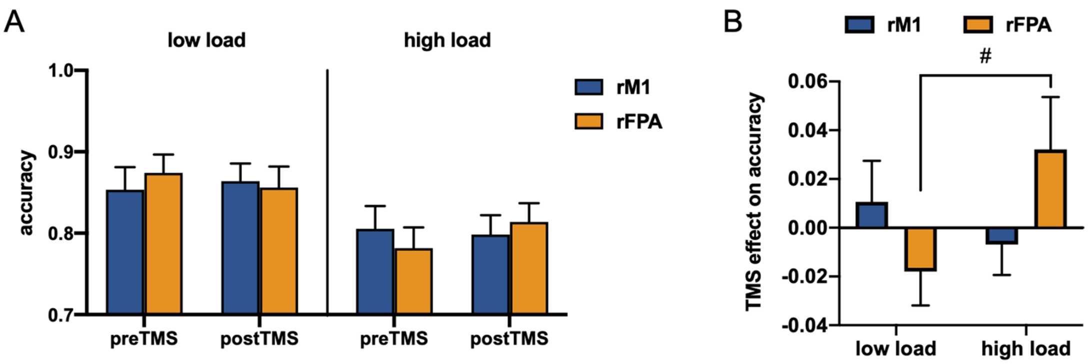

Figure 3. Accuracy of the letter detection task. (**A**) Average accuracy of all conditions. (**B**) The TMS effect of detection accuracy (post TMS accuracy minus pre TMS accuracy). The rFPA TMS effect tended to be bigger in the high load condition than in the low load condition. # Represents a marginal significance level of 0.0072.

10 and 200 deg/s^2. The interception between the best fitting regression line and a horizontal line parallel to x-axis with a value of mean velocity of the baseline interval was marked as the pursuit onset. The procedure was basically the same as the method in the previous studies (Schütz, Braun, & Gegenfurtner, 2007; Schütz et al., 2010). Finally, the pursuit onset of each median trace was inspected manually. Moreover, we computed the eye velocity gain for every 40 ms from the stimuli movement onset to end of the movement, such as 0 to 40, 40 to 80, 80 to 120, 120 to 160, 160 to 200, 200 to 240, 240 to 280, 280 to 320 ms, and etc. Eye velocity gain was calculated by dividing the mean eye velocity by the stimulus velocity. Besides the velocity gain, we have also checked saccade number per trial and sum of saccade amplitude per trial.

For the statistical analysis, 2 × 2 × 2 three-way ANOVA was conducted using pre-post TMS (pre vs. post), TMS site (rFPA vs. rM1), and attentional load (low vs. high) as factors. Given the interaction among 3 factors, two 2-way ANOVA using pre-post and TMS site as factors were conducted for the low and high demanding load conditions separately. TMS effect was computed by subtracting measurement data before the TMS from those after the TMS. Further pairwise comparisons were conducted upon the significant interaction in the 2-way ANOVA.

Results

Accuracy of the letter detection task was analyzed to evaluate the detection task performance. Accuracy of high load condition was significantly lower than that of the low load condition ($F(1, 15) = 16.085$, $p = 0.001$, $\eta^2_p = 0.517$; Figure 3A), confirming a successful manipulation of the attention demanding level that was endowed on the pursuit target. Importantly, the ANOVA revealed a significant interaction among three factors ($F(1, 15) = 4.992$, $p = 0.041$, $\eta^2_p = 0.250$), indicating a differential modulatory effect of the rFPA TMS on the low and high load detection task. To investigate the interaction in details, we computed the TMS effect by subtracting the accuracy before the TMS from the accuracy after the TMS. The ANOVA of the TMS effect revealed a significant interaction ($F(1, 15) = 4.992$, $p = 0.041$, $\eta^2_p = 0.250$) and further comparison revealed no difference of the rM1 TMS effect between the low and high loads ($t(15) = 0.972$, $p = 0.347$), but the rFPA TMS effect tended to be bigger in the high load condition than in the low load condition ($t(15) = -1.934$, $p = 0.072$). These results indicate that the effect of the TMS over the rFPA on the letter detection performance is related to the attention demanding level.

For the pursuit performance, we first checked the velocity gain. To evaluate the rFPA TMS effect on the pursuit gain, trials with both correct and wrong responses of the detection task were included in the analysis. The pursuit latency data did not show any significant effects, so it was reasonable to check the eye velocity traces relative to the stimuli movement onset. Checking the eye velocity gain for every 40 ms since the stimuli movement onset, we found significant 3-way interactions in the 200 to 240, 240 to 280, and 280 to 320 ms time windows, that is the pursuit gain in these time windows were modulated by the TMS over the rFPA, whereas the TMS over the rM1 did not. Thus, we collapsed these time windows into a wider window of 200 to 320 ms. Figure 4A shows the eye velocity gain traces with high attentional demanding task from a representative subject and the rectangle in Figure 4A represents the 200 to 320 ms time window. Average pursuit gain in the 200 to 320 ms analysis showed a significant interaction among three factors ($F(1, 15) = 16.887$, $p = 0.001$, $\eta^2_p = 0.530$; Figure 4B), suggesting differential TMS effects for the rFPA and rM1 in the low

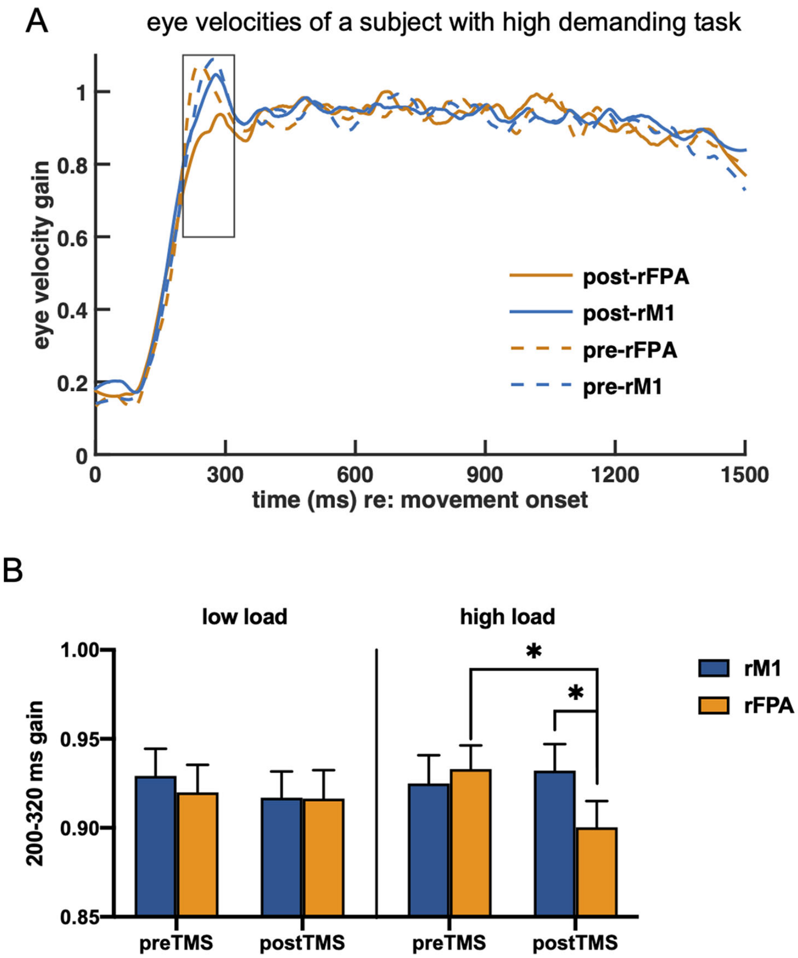

Figure 4. Eye velocity gain. (**A**) Representative eye velocity traces with high attentional demanding task before and after the TMS stimulation. (**B**) The average eye velocity gain in the 200 to 320 ms time window since the stimuli movement onset. * Represents a significance level of 0.05.

and high load conditions. Furthermore, we conducted 2-way ANOVA separately for the low and high attention demanding condition. No significant effects were found in the low attention demanding condition. However, a significant interaction between pre-post and TMS site was found in the high attention demanding condition ($F(1, 15) = 14.053$, $p = 0.002$, $\eta^2_p = 0.484$). Following comparison revealed significant lower gain after the rFPA TMS compared with pre-rFPA TMS ($t(15) = -2.937$, $p = 0.010$), and compared with that after the rM1 TMS ($t(15) = -2.711$, $p = 0.016$). In order to check whether the correctness of the response interacted with the rFPA TMS effect, we have also analyzed the 200 to 320 ms gain in response correct trials only. Statistically, there were no difference between the results of the 200 to 320 ms gain in all trials and that in response correct trials. Moreover, in the present study, low and high demanding tasks used blocked design and the target letter appeared 400 to 800 ms since the stimuli movement onset, which was after 200 to 320 ms time window. Hence, we think that low and high demanding task influenced the pursuit regardless of correct or wrong response trials at least before the target appeared. Thus, we reported the results for all trials. Our results revealed that the TMS over the rFPA reduced the eye velocity gain 200 to 320 ms after the stimuli movement onset. These results showed the rFPA TMS significantly reduced the pursuit gain in the high load condition and further demonstrated that the rFPA TMS effect is modulated by the attention demanding level of the detection task.

To evaluate the relationship between perceptual and motor changes induced by TMS, we computed rFPA TMS effect on the eye velocity gain and then ran a correlation analysis between the rFPA TMS effects on the pursuit gain and attention demanding task. We found a significant correlation between the rFPA TMS effect on the accuracy of attention demanding task and pursuit gain with the high demanding task ($r = 0.805$, $p < 0.001$; see Figure 5). To evaluate the stability of this correlation, we applied the bootstrap method using 10,000 iterations and found 95% confidence interval

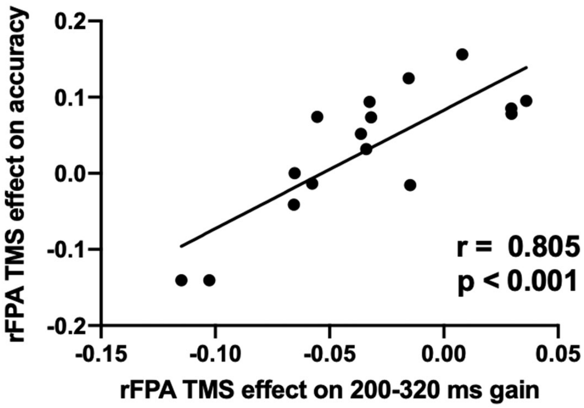

Figure 5. Correlation between the rFPA TMS effect on the pursuit gain and accuracy of the attention demanding task when the attention demanding task had high level.

was [0.508 to 0.927], suggesting the reliability of the correlation. The correlation showed that individuals who showed less impairment demonstrated bigger benefit induced by the TMS over the rFPA, suggesting the TMS over the rFPA modulated either the pursuit gain or the letter detection performance.

Checking the eye velocity gain through the end of the stimuli movement, we found the main effect of the attentional load from the 1200 to 1240 ms time window to the end. Thus, we collapsed these time windows into a wider time window, 1200 to 1500 ms, and analyzed the pursuit gain in this wider time window, 1200 to 1500 ms eye velocity gain showed higher gain in the high load condition (0.894) compared with low load condition (0.874; $F(1, 15) = 18.868$, $p = 0.001$, $\eta^2_p = 0.557$; Figure 6A), suggesting less anticipatory stopping of the pursuit with high attentional load. Anticipatory stopping may be due to fixed duration of the stimuli movement and limit of the display size. Our data indicated high attentional load helped to reduce such anticipatory stopping the pursuit. This is in line with previous finding that the attention task endowed on the pursuit target helps the pursuit. In addition, we checked whether increasing the attentional load would affect the saccadic intrusion during the pursuit. No significant TMS-related results were found for the saccadic frequency. However, there was a main effect of attention load for the sum of the saccade amplitude per trial ($F(1, 15) = 6.931$, $p = 0.019$, $\eta^2_p = 0.316$), indicating smaller amplitude of saccades were produced in the high load condition (1.247) than in the low load condition (1.348). Together with less anticipation in pursuit stopping, our results demonstrated that endowing higher attentional load on the pursuit target improves the pursuit. However, caution should be taken because the magnitude of the load effect is small, presumably because attention at the pursuit target was already facilitated in the low load condition.

Discussion

This study investigated the role of the right FPA in the interaction between smooth pursuit eye movements and attention. To do it, attention demanding task was endowed on the pursuit target and neural activity of the right FPA was interfered by the TMS. Then, the pursuit and attention task performance after the right FPA stimulation were compared with the control site (right primary cortex, rM1) stimulation. We found the rFPA TMS modulated the pursuit and attention task only in the high load condition. In details, the rFPA stimulation lowered the pursuit gain 200 to 320 ms after the movement onset, whereas it tended to improve the attention task performance. Moreover, individuals who showed less impairment of the pursuit gain demonstrated bigger benefit of the attention task induced by the rFPA TMS. These results provided evidence that the rFPA is directly involved in distributing attentional resources between tasks.

Importantly, we found that the TMS over the right FPA modulated the pursuit gain of 200 to 320 ms after the stimuli movement onset in the high load condition. The FPA is directly involved in the control of the pursuit in human (e.g. Petit & Haxby, 1999; Rosano et al., 2002). Our finding of reduced pursuit gain by the FPA TMS supports that the FPA contributes to the gain control of the pursuit. First, it is important to check the reliability of the FPA TMS effect found in the present study because of the small magnitude of the FPA TMS effect. We found about 3.5% of decrease in the 200 to 320 ms time window when the TMS was applied to the rFPA in the high-demanding condition. In spite of the small magnitude, the FPA TMS effect is comparable to other studies in magnitude. Nuding et al. (2009) applied 10 Hz TMS for 500 ms over the left and right FPA and they found that the TMS over the FPA induced 4.3% decrease in steady-state gain (mean eye velocity reduced from 16.1 to 15.4 deg/s) for visually guided pursuit, which was small in magnitude but highly significant. In addition, Gagnon et al. (2006) found about 4.7% of gain decrease when the TMS was delivered during mid-cycle movement, although they found 43.7% increase in the new pursuit direction when the TMS applied at the target turnaround. In the study of Gagnon et al. (2006), the FPA TMS site was localized according to individual's fMRI signal while the participants performed smooth pursuit and fixation task. Besides, Sack et al. (2009) compared four different ways of determining the parietal TMS site, guided by individual fMRI, MRI, Talairach coordinates from a previous literature, and the 10–20 EEG System (P4), and investigated optimal sample size for these different ways. They found that 5 participants were sufficient for the fMRI-guided approach, 9 participants for the MRI-guided approach,13 participants for the Talairach

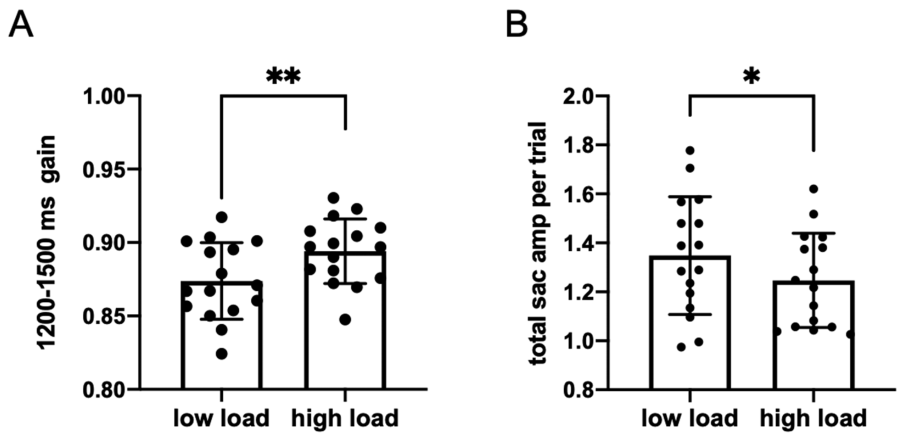

Figure 6. Effect of the attentional load. (**A**) Velocity gain in the 1200 to 1500 ms time window (last 300 ms of the pursuit). (**B**) Sum of saccade amplitude per trial. * Represents a significance level of 0.05 and ** represents a significance level of 0.01.

coordinates, and 47 participants were necessary for the P4 TMS stimulation. According to this study, 16 participants used in the current study are enough for investigating the role of the rFPA. Taken together, the small magnitude of the FPA TMS effect in the present study is reliable. Finding of reduced eye velocity gain is consistent with previous TMS studies that demonstrated the role of the FPA in the pursuit gain control (Gagnon et al., 2006; Nuding et al., 2009). In these previous studies, observers made smooth pursuit eye movements only without any secondary attentional task. In contrast, our observers conducted a letter detection task in addition to the pursuit task. Hence, the TMS over the FPA enabled us to study the role of the FPA in the pursuit and attention concurrently. Behavioral studies have established close relationship between the pursuit and attention (Acker & Toone, 1978; Clementz et al., 1990; Hutton & Tegally, 2005; Kerzel et al., 2009; Stubbs et al., 2018). Here, attention on the pursuit target was successfully manipulated by the letter detection task, as shown by the lower accuracy of letter detection in the high load condition. Importantly, we found the effect of the rFPA TMS on the pursuit gain in the high load condition, where the letter detection task required high level of attentional resources. In contrast, no effect of the rFPA TMS on neither the letter detection nor the pursuit was observed in the low load condition. Considering the role of the FPA in the pursuit gain control (Gagnon et al., 2006; Nuding et al., 2009), the pursuit gain control by the FPA may be compensated by attention in the low load condition. However, in the high load condition, there may be no sufficient attentional resources that could compensate for the FPA TMS effect on the pursuit due to high level of attentional consumption by the letter detection task, resulting in evident pursuit gain reduction by the FPA TMS. This argument is acceptable because endowing attention on the pursuit target is not necessary to mean that attention is allocated to the pursuit task. Average data over the participants showed the FPA stimulation tended to benefit the letter detection only if the letter detection task had high level of attentional load, establishing a beneficial role of the FPA in the letter detection. It seems that the suppression of the FPA, induced by the cTBS method (Huang et al., 2005; Chung et al., 2016), biased attentional resources to the detection task, consistent with attention resource sharing mechanism (Navon & Gopher, 1979). Interestingly, the FPA TMS effects correlation analysis showed that individuals who showed less impairment on the pursuit gain induced by the rFPA TMS demonstrated bigger benefit on the detection performance induced by the rFPA TMS. It seems to contradict the finding from the mean data. However, these individual different results also demonstrated the rFPA TMS effect with high attentional demanding task, because no correlations were found for low demanding tasks. Moreover, the TMS over the rFPA may have modulated either the pursuit gain or the letter detection performance. In other words, the rFPA is involved in both the pursuit and attention demanding task and can flexibly contribute to the pursuit or attention demanding task. In all, our results demonstrate that the gain control by the FPA may be mediated by attention.

On the other hand, a higher attention demanding level improved pursuit performance, as evidenced by higher velocity gain in stooping period (1200-1500 ms since movement onset) and smaller sum of saccades amplitude per trial, in line with the studies demonstrating that facilitating attention at the pursuit target improves overall pursuit performance (Clementz et al., 1990; Stubbs et al., 2018). It has been proposed that the pursuit stopping is affected by active prediction of the upcoming end of the target (Missal & Heinen, 2017). Compared with low load detection task, high load detection task diminished the anticipatory stopping of the pursuit. Besides, we observed anticipatory pursuit response before the pursuit initiation in all conditions as well. This might be due to the experimental design of the present study where the stimuli were presented at the left or right field of the display and always moved toward the display center after a random period of the fixation duration at a constant velocity, resulting in high predictability of the direction and speed of the stimuli movement. However, we did not find any significant effect on the anticipatory pursuit. Together with anticipatory stopping, the level of attention demanding influenced anticipatory pursuit, but only the anticipatory stopping. Additionally, the sum of saccades amplitude per trial was lower in the high load condition, suggesting facilitating attention at the pursuit target helped the pursuit. However, such difference between the high and low load conditions was small in magnitude, which may be related to the current experimental design where attention was facilitated by the letter detection task in both low and high load conditions.

Our results have implications for the role of the FPA in the interaction between the pursuit and attention. In this interaction, it seems that the FPA is responsible to distribute attentional resources between the pursuit and other attention-demanding tasks. Especially when attentional resources are exhausted, the suppression of the FPA impairs the pursuit and tends to improve attention task and the TMS modulation differs across individuals, suggesting that the FPA contributes to attentional allocation between the pursuit and other attention demanding task and its contribution differs across individuals.

Keywords: smooth pursuit eye movements, transcranial magnetic stimulation, frontal pursuit area, attentional allocation

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