Title: Corticospinal excitability during preparation for an anticipatory action is modulated by the availability of visual information.

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Abstract

In order to intercept rapidly moving objects people must predict the right time to initiate their actions. The timing of movement initiation in interceptions is thought to be determined when a perceptual variable specifying time-to-contact reaches a criterion value. If a response needs to be aborted, the performer must make a decision prior to this moment. It has been recently shown that the minimal time to suppress an anticipatory action takes longer during motion extrapolation than during continuous visual information. In Experiment 1, we sought to determine whether or not the availability of visual information would: a) affect the latency to inhibit an anticipatory action, and b) modulate the level of excitability in the motor cortex (M1). The behavioral results showed that the absence of visual information prolonged the latency to stop the movement as previously reported. The neurophysiological data indicated that corticospinal excitability levels were affected by the availability of visual information. In Experiment 2, we sought to verify whether corticospinal excitability levels would also differ between the two visual conditions when the task did not involve response suppression. The results of Experiment 2 indicated that excitability levels did not differ between visual conditions. Overall, our findings indicated that the build-up of motor activation can also play a role in determining different latencies to inhibit an anticipatory action. They also suggest that the build-up of motor activation in the corticospinal pathways can be strategically modulated to the requirements of the task during continuous visual information.

Keywords: anticipatory timing, corticospinal excitability, inhibition, motor preparation.
Introduction

A rapidly executed interception of a moving object, like a service return in tennis, needs to be initiated at the right moment if an effective interception is to occur (Tresilian 2005; Zago et al. 2009). Initiation and subsequent control of these actions has been a vigorous area of research (Merchant and Georgopoulos 2006; Zago et al. 2009). Several models have been developed and all propose that motor commands are initiated when a visually perceived variable associated with the target (e.g., its time-to-contact) reaches a criterion value (Tresilian 2005; Zago et al. 2009): evidence suggests that this event occurs between 150 and 200 ms prior to movement onset (Benguigui et al. 2003; Marinovic et al. 2009c). If a person decides to suppress a brief interceptive movement or to change the response they have prepared, they need to make appropriate adjustments prior to the occurrence of the initiating stimulus event (Marinovic et al. 2009a; b).

Relatively little attention has been paid to people’s ability to abort interceptions. In a preliminary study (Marinovic et al. 2009a) we found that the minimum time needed to effectively suppress an interception in response to a stop stimulus was no less than 200 ms prior to movement onset, consistent with the idea that suppression must be effected before the initiating stimulus event occurs. Suppression of a prepared action is thought to involve a process that inhibits the program or pattern generator responsible for generating descending motor commands (Coxon et al. 2006; van den Wildenberg et al. 2010). The ability of an inhibitory process to successfully suppress the execution of a response will depend not only upon the time of its arrival at the program circuits, but also upon the activation level of those circuits (van den Wildenberg et al. 2010). In reaction time tasks it is known that preparatory activation of the command generating program circuits builds
up in anticipation of the initiating stimulus, reaching a maximum at the anticipated time of the stimulus - a process known as temporal preparation (Requin et al. 1991). Previous research has presented evidence consistent with the idea that a similar temporal preparation process is involved in interceptive actions (Tresilian and Plooy 2006). Thus, an inhibitory signal arriving at the program circuits close to the moment of the initiating stimulus event would need to counteract a maximal level of activation.

In a recent report (Marinovic et al. 2010), we described a finding that may be interpreted in terms of differential levels of preparatory activation of program circuits. Participants performed a task in which they were required to make a response (button press) at the moment a moving target reached a designated location (coincidence-anticipation) task. Like interceptive actions, this type of task requires that the response be initiated at the right time in order to achieve temporal coincidence and initiation must be triggered by some stimulus event that is predictive of the target’s arrival at the designated location (see Tresilian, 1995, for review). We studied participant’s ability to suppress the response under two conditions: a full view condition in which the target was visible up to the designated location and an occluded view condition in which the target was not visible over the last part of its path (see Methods). Suppression times were significant longer (≈ 60 ms) in the occluded view condition. It is possible to interpret this result as being due to greater levels of preparatory activation in the response circuits in the occluded view condition. The plausibility of this interpretation is based on the following reasoning. During temporal preparation activation is thought to build up as the anticipated time of response initiation approaches and can only be sustained at an optimal level for short periods (Los and Van den Heuvel 2001). The greater the accuracy with
which the time of response initiation can be anticipated, the shorter the time for which
readiness need be maintained at the optimal level (Alegria 1974; Muller-Gethmann et al.
2003) as the period of preparation can be coordinated with the time at which the response
initiating signal occurs. Performance is typically very precise (low variability) in
interception and coincidence-anticipation tasks under full view conditions (Schmidt
1969), but less precise when the target is occluded (reviewed in Tresilian 1995). This
implies that the time of response initiation can be anticipated with greater precision in full
view conditions, but less precisely in occluded view conditions. In order to accommodate
this lack of precision, the period during which preparatory activity is sustained at a high
level could be extended as found in earlier studies (Alegria 1974; Carlsen and Mackinnon
2010; Muller-Gethmann et al. 2003). A sustained high level of activity prior to movement
initiation would take longer to suppress, which would lead to greater suppression times in
the occluded view condition.

We report the results of two experiments in which we attempted to test this idea.
Participants performed both a coincidence-anticipation task (full view condition) and a
prediction-motion task (occluded view condition). Their ability to suppress responses was
examined under these conditions. In experiment 1, we sought to replicate our previous
behavioral finding that the minimum suppression time is greater during occlusions and
also looked for direct evidence for higher levels of response-related activity by testing
corticospinal excitability using single-pulse transcranial magnetic stimulation (TMS)
(Chen et al. 1998; Leocani et al. 2000). In experiment 2, we sought to examine whether
we could find evidence of higher levels of corticospinal excitability when the task did not
involve response suppression.
Material and Methods

Subjects

Twelve volunteers participated in the experiments (four of whom took part in both experiments) and all gave their informed consent prior to commencement of the study, which was approved by the local Ethics Committee of the University of Queensland. All participants reported normal or corrected to normal vision and stated they were right handed. Their ages ranged from 21 to 34 years (mean = 29.3 years, SD = 5.4 years).

Experiment 1

Task and apparatus

Participants were seated in a comfortable chair in front of a computer screen with support for the arms and hands as depicted in Figure 1. Support for the hands was purposefully built to allow the participants to remain comfortable with their hands in a pronated position throughout the experiment. The participants were required to abduct their right index finger against a force transducer, placed beside their right hand on the hand rest, at the precise moment they judged a moving target (50 x 25 pixels) would make contact with a stationary target (25 x 50 pixels) positioned at the right side of a monitor screen as shown in Figure 2. In one block of trials, occluded view (OV), the target disappeared from view 500 ms prior to reaching the stationary target as shown in Figure 2A. In another block of trials, full view (FV), the moving target was visible throughout its entire trajectory until it reached the stationary target at the right side of the monitor screen as shown in Figure 2B. In both conditions the moment of contact was indicated by the stationary target changing from green to red. A stop-signal would appear on the screen in
40% of the trials in both conditions as shown in Figure 2C. The participants were instructed to remain at rest when this event occurred. The moving target took 2000 ms to move from the left to the right side of a 19” monitor screen (85 Hz refresh rate, 1024 x 768 resolution) located 0.9 meters away from the participants as shown in Figure 1. Visual stimuli were generated with Cogent 2000 Graphics (http://www.vislab.ucl.ac.uk/cogent_2000.php) running in MATLAB 7.5.

Figure 1. Experimental setup (not to scale). The participant was seated in front of a monitor screen which displayed the visual stimuli. The figure-of-eight coil which delivered the magnetic stimulus was held by the experimenter (not shown in the figure) over the left motor cortex.
Procedures and design

Prior to the experimental blocks, the participants were trained to abduct their index fingers at the correct time. During practice they initially performed 50 trials without stop signals and then another 24 trials where each stop-signal was pseudorandomly presented twice (practice was provided for both blocks). Feedback about inhibition failures (for stop-signal trials) and about temporal error (go trials with no TMS) was provided during training and experimental blocks. The participants were informed that they failed to inhibit their actions during no-go trials when force transducer levels exceeded 3 standard deviations from baseline levels. The experiment was run in two blocks: a) occluded view, and b) full view. In the occluded view block the moving object disappeared from view 500 ms before its arrival at the contact point as shown in Figure 2A. In the full view block the moving object was seen until it reached the contact point as shown in Figure 2B. Following practice, half the participants began the experiment with block a, and half with block b. The participants performed 150 trials for each experimental block (300
total). In each block, on 60 trials (40% of total), a red stop sign (stop-signal) suddenly appeared on the screen (210 x 210 pixels) as shown in Figure 2C and it served to inform the participants that they were to inhibit the initiation of their movements. Although the frequency of stop-signals in the present study was lower than that used in our previous studies (Marinovic et al. 2009a; Marinovic et al. 2010), we anticipated that the 40% chance of a stop-signal would be sufficient to create an expectation on the participants to halt their actions. The stop-signal appeared pseudorandomly on the monitor screen at various times (100, 134, 171, 205, 241, and 276 ms) prior to the exact moment in which the moving target contacted the stationary target and remained at its initial position until the end of the trial. We presented 10 trials for each stop-signal interval in each block. Feedback about whether or not they succeeded to inhibit their movements after stop-signal trials was provided to motivate the participants to attend to the stop-signal. The remaining trials were go trials where the participants were required to be as accurate as possible to synchronize the onset of their movements with the arrival of the moving target at the contact point. On 40 of the go trials (26.6% of total) single-pulse transcranial magnetic stimulation (TMS) was delivered to the left primary motor cortex at the optimal position to elicit a motor evoked potential (MEP) in the first dorsal interosseous (FDI) muscle of the right hand. TMS was delivered at four intervals (201, 173, 146, and 120 ms) prior to the exact moment at which the moving target contacted the stationary target (expected time of movement onset) in the full view and occluded view conditions. We delivered TMS on 10 trials for each of the four intervals. In the remaining go trials (33.3% of total) no TMS was delivered. For these go trials the participants were given feedback about their temporal error to initiate their movements with the arrival of the
moving target at the contact point. Feedback for these trials was provided to encourage
the participants to achieve optimal performance and avoid using strategies that could
increase their chances to inhibit their actions more easily (e.g. delaying movement onset
to increase the stop-signal interval).

TMS stimulation

Before the participants were given instructions about the task, the TMS intensity was
established for each participant by finding the lowest stimulation intensity that could
reliably elicit a peak-to-peak MEP of approximately 1mV in the first dorsal interosseous
muscle (primary agonist in the task). This criterion was particularly preferred for this
experiment as it allows for the detection of both an increase and decrease in excitability
(Bestmann et al. 2004). The position of the coil over the specific site of stimulation was
held in place by one experimenter. In order to increase the spatial accuracy of the
stimulation over the target area we used an image-guided frameless stereotactic
neuronavigation system (StealthStation, Medtronic, USA), which provided online
guidance to the person holding the coil in place. MEPs were recorded from the first
dorsal interosseous (FDI) and the abductor digiti minimi (ADM) of the right hand using
disposable Ag-AgCl electrodes. The EMG signal was amplified, band-pass filtered
between 30 Hz and 1 kHz (Grass P511 isolated amplifier) sampled at 2000 Hz and stored
on computer. The torque transducer data was time locked to the collection of the EMG
signal and also sampled at 2000 Hz.
Data analysis

In Experiment 1, the variables of interest were the presence of movement during stop-signal trials, which was indicated by torque level exceeding 3 standard deviations from baseline levels for more than 40 samples. Amplitude of the mean peak-to-peak MEP expressed as a proportion of those at rest. Temporal error, defined as the difference between movement onset and the time the moving target arrived at the designed location (negative = early). Variable temporal error, defined as the standard deviation of the temporal error over a series of trials.

Data regarding the presence of movements during stop-signal trials was first analyzed through a repeated measures analysis of variance. As the percentage of inhibited trials follows a binomial distribution, we used the arcsine squared root transformation to analyze this variable as recommended by Hogg and Craig (1995). The mean transformed percentage of successful inhibitions were submitted to 2 (view condition: FV and OV) x 6 (stop-signal interval: 100, 134, 171, 205, 241, 276 ms) repeated measures ANOVA. A Tukey HSD post-hoc test, $P > .05$, was conducted to determine the locus of significant differences involving more than two means. After this analysis, the non-transformed percentage of inhibited trials was used to obtain inhibition functions. The probability of inhibiting the response for each time at which the stop signal was presented was fitted with a cumulative Gaussian by using a maximum-likelihood fitting procedure. The time required to halt the movement was defined as the point in the inhibition function at which the probability of inhibiting the action was 0.5. The time to inhibit was then corrected for each participant based on the constant temporal error obtained in control trials (trials
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without a stop signal or TMS). The corrected values in which the inhibition functions reached 0.5 for the two experimental blocks were then compared using a paired t-test.

To analyze peak-to-peak MEP amplitude, we first calculated the time interval between TMS delivery and the onset of voluntary EMG contraction so that trials could be temporally binned in relation to the actual interval between TMS and voluntary movement onset. Any trial in which voluntary contraction was found to occur before magnetic stimulation was discarded from further analysis. These were more common for stimulations occurring closer to the expected time of arrival of the moving target at the determined contact point. MEP amplitudes were binned into three intervals of equal width (101-150, 151-200 and 201-251 ms). The means of the MEPs amplitude of the temporally binned trials were submitted to 2 (view condition: FV and OV) x 3 (binned interval: 101-150, 151-200 and 201-251 ms) repeated measures ANOVA. A Tukey HSD post-hoc test, \( P \geq .05 \), was conducted to determine the locus of significant differences involving more than two means. Constant temporal error and variable temporal error in both experimental blocks were compared via paired t-tests as only control trials were used to analyze the participants’ performance during go-trials.

Experiment 2

The task, apparatus and procedures were identical to those employed in Experiment 1 with the exception of the following details. No stop-signals were presented during the two experimental blocks (full-view and occluded-view). Therefore, participants were only required to synchronize their movements with the arrival of the moving target at the contact point on the monitor screen. Prior to the experimental session, the participants
performed 50 trials to learn the appropriate time of movement onset and they were informed about their temporal error after all trials. The participants performed a total of 120 trials in each experimental block. In each block, TMS was applied pseudorandomly on 40 trials (33.3% of total) to the left primary motor cortex at the optimal position to elicit a motor evoked potential (MEP) in the FDI muscle of the right hand. The times of single-pulse magnetic stimulation were the same as those used in Experiment 1. For Experiment 2, we recorded EMG data only from the FDI muscle.

Data analysis
In Experiment 2, the variables of interest were: the amplitude of the mean peak-to-peak MEP expressed as a proportion of those at rest and the constant temporal error. The procedures to analyze these variables were the same as those used in Experiment 1. In Experiment 2, due to the lack of data points within the longest interval across all participants we only analyzed two intervals (101-150 and 151-200 ms).

Results
Experiment 1
The mean constant temporal error (SD) for the full view block was -1.9 ms (SD 21.2), whereas for the occluded view block it was -16.6 ms (SD 25.3). A paired t-test failed to show a significant difference between these means, \( t(7) = 1.42, P = 0.196, r = 0.22 \). This result seems to suggest that there was no predisposition for the participants to initiate their actions earlier or later than expected in a particular block. The mean variable temporal error (SD) was 35.0 ms (SD 11.1) in the full view block and 56.6 ms (SD 14.3)
in the occluded view block. The paired t-test revealed a significant difference between these means, $t(7) = 6.98, P < 0.001, r = 0.93$. As expected (see Introduction) the participants showed greater variability to time their responses in the absence of continuous visual motion information.

The repeated measures ANOVA on the transformed percentage of inhibited trials found a significant main effect of viewing block, $F(1,7) = 14.3, P = 0.007, \eta^2_p = 0.67$. This main effect indicates that the participants suppressed more movements in the full view block than in the occluded view block. There was also a significant main effect of stop-signal interval, $F(5,35) = 48.74, P < 0.001, \eta^2_p = 0.87$. The post-hoc test of this effect showed that the success rate to suppress movement initiation increased in both blocks as the time available to halt the actions increased. Furthermore, the analysis of variance also showed that the interaction between viewing block and stop-signal interval was statistically significant, $F(5, 35) = 5.46, P < 0.001, \eta^2_p = 0.44$. The post-hoc comparisons for this interaction indicated that the participants inhibited more movements in the full view block at 171, 205, 241, and 276 ms prior to the arrival of the movement target at the arrival location. At earlier times, however, there were no differences between full view and occluded view blocks as shown in Figure 3A. This pattern of results is very similar to that we reported previously with a similar anticipatory task (Marinovic et al. 2010) where no magnetic stimulation was employed and the probability of response suppression was relatively higher than that we used in the present study.
Figure 3. A - Mean percentage of successfully inhibited responses as a function of the stop-signal (SS) interval. Black circles represent the full view block (FV). Grey circles represent the occluded view block (OV). * Marks significant contrasts between FV and OV. Error bars represent 95% confidence intervals. B - Inhibition functions for the group data. The curves are the cumulative Gaussian functions that best fit the data. The black lines represent the inhibition function for the full view block (FV). The grey lines represent the inhibition function for the occluded view block (OV). Error bars represent the standard error of the group mean.

In Figure 3B are shown the inhibition functions for the group mean. As shown in Figure 3B, a 0.5 probability of inhibiting a prepared response occurred later for the occluded view condition compared with the full view condition. This pattern was consistent for all participants. Following Slater-Hammel procedures (1960), the mean constant temporal error of each participant was used to adjust the time required to inhibit 0.5 of the responses. The mean (SD) adjusted time to inhibit a response in the full view block across participants was 173.8 ms (SD 35.5), whereas in the occluded view block the mean was 227.7 ms (SD 33.6). A paired t test comparing these means showed that the minimum time required to suppress the response was significantly shorter in the full view than in the occluded view block, $t(7) = 5.68, P < 0.001, r = 0.82$. This difference in suppression time between full view and occluded view blocks ($\approx 54$ ms) is similar to that
we reported previously (Marinovic et al. 2010), even though the probability of having to inhibit an upcoming action was lower in the present study.

Figure 4 shows peak-to-peak MEP amplitude ratio for the two muscles recorded (FDI and ADM) as well as the mean time of stimulation in each experimental condition. The repeated measures ANOVA on the peak-to-peak MEP amplitude of the FDI muscle (see Fig. 4A) showed a significant main effect of viewing block, $F(1,7) = 6.67, P = 0.036$, $\eta^2_p = 0.49$. This main effect of viewing block indicates that the participants reached significantly higher levels of excitability in the occluded view block than in the full view block. There was also a significant main effect of time of stimulation, $F(2,14) = 30.06, P < 0.001$, $\eta^2_p = 0.81$. This main effect of time of stimulation shows that excitability levels increased for the FDI muscle for both blocks as the time of stimulation became closer to movement onset time. There was also a significant interaction between viewing block and time of stimulation for the FDI muscle, $F(2,14) = 4.40, P = 0.032$, $\eta^2_p = 0.39$. A post hoc test of this interaction indicated that excitability was higher in the occluded view block than in the full view block at the shortest time of stimulation (101-150 ms). For the ADM muscle (see Fig. 4B), the repeated measures ANOVA showed a significant effect of viewing block, $F(1,7) = 6.10, P = 0.042$, $\eta^2_p = 0.47$, but no main effect of stimulation time, $F(2,14) = 0.10, P = 0.906$, $\eta^2_p = 0.01$. This significant main effect of viewing block seems to suggest that there was a smaller amount of corticospinal suppression on M1 for the ADM muscle in the occluded view block, which was not contingent upon the time of stimulation. There was no significant interaction between viewing block and time, $F(2,14) = 0.10, P = 0.905$, $\eta^2_p = 0.01$. 


Figure 4. A - B: Mean normalized peak-to-peak MEP amplitude for FDI (A) and ADM (B) muscles in the two blocks as a function of time of stimulation. C: Mean time of stimulation in each temporal bin. Error bars represent the 95% confidence intervals.
As the mean time of stimulation between conditions could affect the results (e.g. a lower mean time of stimulation could lead to higher corticospinal excitability), we also compared the mean time of stimulation in both blocks to examine whether a bias was evident. The repeated measures ANOVA on the mean time of stimulation showed no significant main effect of viewing block, $F(1,7) = 0.61, P = 0.460, \eta^2_p = 0.08$. This result indicates that there was no evident trend in relation to the time of stimulation between viewing blocks. The analysis of variance found a significant main effect of time of stimulation, $F(1,14) = 574.50, P < 0.001, \eta^2_p = 0.99$. The post hoc test showed that each mean time of stimulation within each bin was significantly different from each other. This main effect simply shows, as expected, that the mean time of stimulation was different between the three temporal bins. There was no interaction between viewing block and time of stimulation, $F(2,14) = 3.67, P = 0.052, \eta^2_p = 0.34$.

In order to determine whether baseline pre-TMS EMG activity was associated with differences in MEP amplitude, we calculated the root mean squared EMG activity for 250 ms prior to TMS in both experimental blocks. For the FDI muscle, a paired t-test comparing the mean pre-TMS EMG activity during full view (0.0060 SD 0.0012 mV) and occluded view (0.0068 SD 0.0019 mV) blocks failed to detect a significant difference between the means, $t(7) = 1.26, P = 0.246, r = 0.18$. In addition, the 99% confidence interval for the difference between means included zero, CI = [-0.003 to 0.002], which indicates that the true value for this difference was indeed very small. For the ADM muscle, the paired t-test comparing the mean pre-TMS EMG activity for the full view (0.0068 SD 0.0032 mV) and occluded view (0.0071 SD 0.0038 mV) blocks also failed to find a significant difference between means, $t(7) = 1.04, P = 0.332, r = 0.13$. Again the
99% confidence interval for the difference between means included zero as a possible value which suggests any possible difference between means was negligible (99% CI = [-0.005 to 0.005]). Thus, not only did we fail to detect significant difference between blocks in relation to pre-TMS EMG activity (which seems to be in agreement with the confidence intervals for the difference between means) but also the values observed for both blocks were very small and well within previously reported values for RMS EMG at rest (e.g. Moller et al. 2009). These results suggest that differences in MEP amplitude between full view and occluded view blocks were unlikely to be caused by an increase in pre-TMS EMG activity.

We also analyzed EMG amplitude and time to peak EMG during control and TMS trials to test whether our results could have been affected by the systematic programming of different responses during motor preparation. Table 1 shows the mean values of EMG amplitude and time to peak amplitude of the rectified and low-pass filtered (50 Hz cut-off) EMG for the full view and occluded view blocks during control and TMS trials in Experiment 1. A 2 (type of trial: control and TMS) by 2 (view condition: full view and occluded view) repeated measures ANOVA on the EMG amplitude showed no main effect of type of trial, F(1,7) = 0.74, P = 0.415, $\eta^2_p = 0.09$, nor viewing condition, F(1,7) = 0.01, P = 0.895, $\eta^2_p = 0.03$. The interaction between type of trial and viewing condition was also non-significant, F(1,7) = 1.01, P = 0.345, $\eta^2_p = 0.12$. Similarly, the analysis of variance on the time to peak EMG revealed no significant main effect of type of trial, F(1,7) = 1.40, P = 0.278, $\eta^2_p = 0.16$, nor viewing condition, F(1,7) = 0.002, P = 0.961, $\eta^2_p = 0.00$. The interaction between type of trial and viewing condition was also non-significant for this variable, F(1,7) = 2.32, P = 0.175, $\eta^2_p = 0.25$. 
Thus, different levels of corticospinal excitability between full view and occluded view blocks are unlikely to be explained by differences in the prepared motor output as any effect there could have been there was too small to be detected.

Table 1: Mean (SD) values of EMG amplitude and time to peak EMG in Experiment 1 and 2.

<table>
<thead>
<tr>
<th>Variable</th>
<th>FV control</th>
<th>OV control</th>
<th>FV TMS</th>
<th>OV TMS</th>
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<td><strong>Experiment 1:</strong></td>
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<td></td>
<td></td>
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<tr>
<td>EMG amplitude FDI (mV)</td>
<td>0.63 (0.37)</td>
<td>0.63 (0.39)</td>
<td>0.64 (0.37)</td>
<td>0.65 (0.38)</td>
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<td>Time to peak EMG FDI (ms)</td>
<td>124.9 (22.3)</td>
<td>134.9 (29.6)</td>
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<td></td>
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</tr>
<tr>
<td>EMG amplitude FDI (mV)</td>
<td>0.66 (0.50)</td>
<td>0.62 (0.52)</td>
<td>0.70 (0.47)</td>
<td>0.68 (0.47)</td>
</tr>
<tr>
<td>Time to peak EMG FDI (ms)</td>
<td>96.7 (45.6)</td>
<td>108.5 (43.2)</td>
<td>78.7 (29.6)</td>
<td>81.9 (36.5)</td>
</tr>
</tbody>
</table>

Experiment 2

The constant temporal error in the full view block was -6.9 ms (SD 22.1) and in the occluded view block it was 4.3 ms (SD 26.0). A paired t test of the means obtained in both blocks was not statistically significant, $t(7) = 1.14, P = 0.289, r = 0.15$. This indicates that, on average, the participants initiated their movements at similar times in both experimental blocks. The mean variable temporal error (SD) was 37.8 ms (SD 6.4) in the full view block and 79.3 ms (SD 20.4) in the occluded view block. The paired t-test showed a significant difference between these means, $t(7) = 6.53, P < 0.001, r = 0.92$. As in Experiment 1, this indicates that visual information aided the participants to better time their responses during the full view block.
Figure 5. A: Mean normalized peak-to-peak MEP amplitude for the FDI muscle in the two blocks as a function of time of stimulation. B: Mean time of stimulation in each temporal bin. Error bars represent the 95% confidence intervals.

Figure 5 shows peak-to-peak MEP amplitude ratio for the FDI muscle and the mean time of stimulation in each experimental condition. The repeated measures ANOVA on the peak-to-peak MEP amplitude for the FDI muscle (see Fig. 5A) showed no statistically significant main effect of viewing block, $F(1,7) = 1.65$, $P = 0.240$, $\eta_p^2 = 0.19$. There was, however, a significant main effect of time of stimulation, $F(1,7) = 12.58$, $P = 0.009$, $\eta_p^2 = 0.64$. Once again, this main effect of time of stimulation indicates that
excitability levels for the FDI muscle increased as the time of stimulation became closer to movement onset time. There was no interaction between viewing block and time of stimulation, $F(1,7) = 1.68, P = 0.235, \eta_p^2 = 0.19$. In Experiment 2, therefore, we once again found the effect of time on the excitability levels but failed to replicate the effect of viewing block obtained in Experiment 1, where we found higher corticospinal excitability in the occluded view block. As for Experiment 1, we also compared the mean time of stimulation obtained in the two temporal bins in both blocks. The repeated measures ANOVA on this variable again showed, as expected, a significant main effect of time of stimulation, $F(1,7) = 131.78, P < 0.001, \eta_p^2 = 0.95$. There was no main effect of viewing block, $F(1,7) = 0.82, P = 0.395, \eta_p^2 = 0.10$, which indicates a bias in terms of time of stimulation was unlikely to have occurred. The interaction between viewing block and time of stimulation was also non-significant, $F(1,7) = 0.32, P = 0.584, \eta_p^2 = 0.04$.

The paired t-test comparing baseline pre-TMS EMG activity on FDI in the full view (0.006 SD 0.001 mV) and occluded view (0.007 SD 0.005 mV) blocks was not significant, $t(7) = 0.53, P = 0.606, r = 0.03$. The 99% confidence interval for the difference between means ranged from -0.006 to 0.004, which indicates the possible true value for the difference between blocks was close to zero. In Table 1 are shown the mean values of the rectified and low-pass filtered (50 Hz) EMG amplitude and time to peak EMG for the full view and occluded view blocks during control and TMS trials in Experiment 2. As with Experiment 1, the repeated measures analysis of variance on the EMG amplitude showed no main effects of type of trial (control vs. TMS), $F(1, 7) = 2.67, P = 0.146, \eta_p^2 = 0.27$, and viewing condition (Full view vs. Occluded view), $F(1,7) = 0.85, P = 0.385, \eta_p^2 = 0.11$. The interaction between type of trial and viewing condition
also failed to reach significance, $F(1,7) = 0.29$, $P = 0.607$, $\eta^2_p = 0.04$. The ANOVA on
the time to peak EMG showed a significant main effect of type of trial, $F(1,7) = 12.09$, $P = 0.010$, $\eta^2_p = 0.63$, but failed to show a main effect of viewing condition, $F(1,7) = 3.38$, $P = 0.108$, $\eta^2_p = 0.28$. The interaction term for this variable was non-significant, $F(1,7) = 3.11$, $P = 0.121$, $\eta^2_p = 0.31$. These results indicate that time to peak EMG occurred sooner
during TMS trials than control trials but this effect was independent of the viewing condition. Therefore, the analyses of pre-TMS EMG activity, EMG amplitude and time
to peak EMG seem to indicate that differences between experiments are unlikely to be
due to pre-TMS activity or the prepared motor response.

**Discussion**

Experiment 1 replicated our previous finding that minimum suppression time is greater
when the coincidence timing task involved motion extrapolation (occluded view) than
when it did not (full view). Single pulse TMS was applied on certain trials to assess
whether the level of corticospinal excitability prior to response onset differed between the
occluded view and full view conditions. The results showed that the evoked potentials in
the FDI muscle, primary agonist in the experimental task, were of smaller relative
amplitude in the full view condition than in the occluded view condition. This difference
was not detectable when TMS was delivered more than 200 ms prior to response onset
and was not observed in a muscle unrelated to task performance (abductor digiti minimi).
These findings indicate that task-specific corticospinal excitability was greater
immediately prior to response onset in the occluded view condition. In both conditions,
the MEPs in FDI were greater the shorter the interval between TMS delivery and
movement onset, indicating a build-up of corticospinal excitability immediately prior to response initiation (Chen et al. 1998; Coxon et al. 2006; Leocani et al. 2000; MacKinnon and Rothwell 2000).

The finding that corticospinal excitability (as assessed by relative MEP amplitude) was greater in the occluded view condition is consistent with the hypothesis that greater levels of preparatory response activation are responsible for the longer minimum suppression times in this condition. An inhibitory signal triggered by the stop signal would need to suppress greater program circuit activity in the occluded view condition than in the full view condition. The involvement of the corticospinal system in these processes was demonstrated by Coxon et al. (2006) who showed that the intentional inhibition of anticipatory actions is exerted at a cortical level and that inhibitory networks within M1 contribute to response suppression after a stop-signal is delivered. The results from experiment 1 show that corticospinal excitability reached higher levels and developed more quickly in the occluded vision condition during the interval from 200 to 100 ms prior to response onset (Figure 4A). The hypothesis described in the introduction was that due to greater temporal uncertainty in the occluded view condition, preparatory response related activity would start to develop earlier and be sustained at higher levels for a longer duration in this condition. Although there was evidence for higher levels being sustained for longer, there was no evidence that activation build up began earlier in the occluded view condition as relative MEP amplitudes were similar at times greater than 200 ms prior to response onset. Thus, the hypothesis was only partially supported by the results of experiment 1: rather than starting to develop earlier, response-related activation in the occluded view condition appears to have developed at a faster rate. We
can speculatively suggest that there was an increased inhibitory activity within M1 which reduced the rate of development of response-related activation during the full view block. The fact that we found evidence of decreased excitability levels for the ADM muscle during the full view block in relation to the occluded view block and that generalized inhibition is easier to perform than selective inhibition (Coxon et al. 2007) support this possibility. Further experiments should examine the contribution of excitatory and inhibitory inputs to the overall level of activation within M1 during different viewing conditions (Full view vs. Occluded view).

The results of experiment 2 did not provide any support for the hypothesis that preparatory response-related activity would be greater in the occluded view condition: although relative MEP amplitude was greater on average in the occluded view condition, the difference was not statistically significant. What experiment 2 does indicate is that the differential corticospinal excitability in the different viewing conditions is affected by whether or not the person expects that they might have to suppress the response. When the person is in a task situation in which suppression might be required (experiment 1) differential corticospinal excitability was observed; when suppression was never required (experiment 2), the differential excitability was much reduced (not statistically detectable).

The manipulation of visual information (full view vs. occluded view) in the experiments reported raise the possibility that different visual streams were employed during the different experimental conditions (see Tresilian 1995). There is a body of evidence suggesting that the dorsal visual stream is mainly responsible for vision-for-action, whereas the ventral visual stream is responsible for vision-for-perception (see
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Goodale 2008; Milner and Goodale 2008; Milner and Goodale 2006). One can hypothesize, therefore, that the difference in corticospinal excitability between the conditions may be due to the two conditions involving the dorsal and ventral streams and that the former allows a more controlled build up of response-related activation. Bosco, Carrozzo and Lacquaniti (2008) have recently presented evidence that the dorsal stream provides internal timing signals used for interceptions and its disruption by means of TMS over MT/V5+ can be detrimental to performance in this type of task. Merchant and colleagues (2004a; b) also found evidence that area 7a of monkeys, located in the inferior parietal lobule in the dorsal visual stream, can provide timing signals to trigger interceptions. Our results seem to be consistent with the controlled build-up hypothesis in the sense that when using the dorsal visual system to trigger interceptive actions (Bosco et al. 2008; Merchant et al. 2004a; b), people can maintain (lower) levels of corticospinal excitability which allow for faster response inhibition (van den Wildenberg et al. 2010).

We believe, however, that it would be unreasonable to assume that the relatively long delay (54 ms) to inhibit interceptions during motion extrapolation is caused entirely by differential corticospinal excitability levels given the speed of neurotransmission in the cerebral cortex (e.g. Perez and Cohen 2009). As we have suggested in a previous study (Marinovic et al. 2010), reduced neural resources during mental extrapolation could increase the reaction time to the stop-signal and also contribute to this delay. A combination of neuroimaging (e.g. fMRI and EEG) and behavioral approaches may allow further insight into the underlying mechanisms and processes behind this phenomenon.

In conclusion, the experiments presented here demonstrate that timed responses to a moving target can be suppressed more quickly (as indexed by shorter minimum
suppression times) when the target is visible up to the moment the response is made than when it is occluded from view. Furthermore, shortly prior to response initiation, corticospinal excitability was found to be lower in the full view condition which may have made the anticipatory timing action more easily suppressed in this condition. This reduced corticospinal excitability during the full view condition, however, was more evident when lower levels of activation of M1 favored the success in the task.

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Figure legends

Figure 1. Experimental setup (not to scale). The participant was seated in front of a monitor screen which displayed the visual stimuli. The figure-of-eight coil which delivered the magnetic stimulus was held by the experimenter (not shown in the figure) over the left motor cortex.

Figure 2. Schematic representation of the time course of events during the task. A - Occluded view for go-trials. B - Full view for go-trials. C - Stop-signal trials.

Figure 3. A - Mean percentage of successfully inhibited responses as a function of the stop-signal (SS) interval. Black circles represent the full view block (FV). Grey circles represent the occluded view block (OV). * Marks significant contrasts between FV and OV. Error bars represent 95% confidence intervals. B - Inhibition functions for the group data. The curves are the cumulative Gaussian functions that best fit the data. The black lines represent the inhibition function for the full view block (FV). The grey lines represent the inhibition function for the occluded view block (OV). Error bars represent the standard error of the group mean.

Figure 4. A - B: Mean normalized peak-to-peak MEP amplitude for FDI (A) and ADM (B) muscles in the two blocks as a function of time of stimulation. C: Mean time of stimulation in each temporal bin. Error bars represent the 95% confidence intervals.

Figure 5. A: Mean normalized peak-to-peak MEP amplitude for the FDI muscle in the two blocks as a function of time of stimulation. B: Mean time of stimulation in each temporal bin. Error bars represent the 95% confidence intervals.

Table legend

Table 1: Mean (SD) values of EMG amplitude and time to peak EMG in Experiment 1 and 2.
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