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How does temporal preparation speed up response implementation in choice tasks? Evidence for an early cortical activation

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Abstract

We investigated the influence of temporal preparation on information processing. Single-pulse transcranial magnetic stimulation (TMS) of the primary motor cortex was delivered during a between-hand choice task. The time interval between the warning and the imperative stimulus varied across blocks of trials was either optimal (500 ms) or nonoptimal (2500 ms) for participants' performance. Silent period duration was shorter prior to the first evidence of response selection for the optimal condition. Amplitude of the motor evoked potential specific to the responding hand increased earlier for the optimal condition. These results revealed an early release of cortical inhibition and a faster integration of the response selection-related inputs to the corticospinal pathway when temporal preparation is better. Temporal preparation may induce cortical activation prior to response selection that speeds up the implementation of the selected response.

Descriptors: Corticospinal excitability, Intracortical inhibition, Motor control, Preparation for action, Primary motor cortex, Reaction time

Temporal preparation is known to influence information processing. In choice reaction time (RT) tasks, such an influence becomes manifest through the manipulation of the interval between a warning signal and the imperative stimulus, an interval termed the "foreperiod." RT lengthens as the duration of the foreperiod is increased, provided that this manipulation is performed across blocks of trials (Woodrow, 1914). This finding reveals that (a) temporal preparation is set according to participant's expectations concerning the time of occurrence of the response signal; and (b) the accuracy of this timing decreases as the time separating the precue from the imperative stimulus lengthens (see Requin, Brener, & Ring, 1991, for a review).

In two-choice RT tasks, decision-making models assume that evidence favoring one alternative is integrated over time with a discrete or continuous accumulation until a threshold is reached that triggers the selected response (e.g., Ratcliff & Smith, 2004). In these models, the main relevant parameters are the onset level of information accumulation, the accumulation rate, and the response threshold level (Figure 1A). Temporal preparation may affect specifically one of these parameters (e.g., Bausenhart, Rolke, Seibold, & Ulrich, 2010; Tandonnet, Garry, & Summers, 2010). Transcranial magnetic stimulation (TMS) opens windows on covert response implementation and can be used for deciphering how temporal preparation affects information processing. The present study addressed this issue. In the following paragraphs, we will first sketch the effects of single-pulse TMS (sTMS) on motor cortex and corticospinal excitability. Second, we will summarize results relative to temporal preparation obtained with this technique. Third, we will formulate specific predictions.

TMS of the primary motor cortex can provide insights relative to changes in excitability both within the motor cortex and at the level of the corticospinal pathway (see Reis et al., 2008, for a review). When the response agonists are tonically contracted, sTMS of the cortical zones that control these muscles evokes two events in the ongoing electromyogram (EMG). First, due to the direct or transynaptic (for upper limb effectors) recruitment of corticospinal neurons, sTMS causes a synchronous discharge of the motoneuronal pool reflected by the motor evoked potential (MEP; see Terao & Ugawa, 2002). The MEP is then followed by a silent period (SP) in the ongoing tonic EMG activity. While the initial part of the SP can be a direct consequence of the MEP (refractory period of neurons involved in the MEP, pause in spindle firing, or Renshaw inhibition), the later part results from the recruitment of inhibitory gamma-aminobutyric acid (GABA)-ergic interneurons within the motor cortex (Ni, Gunraj, & Chen, 2007; Ridding & Rothwell, 2007; Schnitzler & Benecke, 1994; Terao & Ugawa 2002; Uncini, Treviso, Di Muzio, Simone, & Pullman, 1993). When stimulation intensity is constant, variations in MEP amplitude thus reflect changes in the excitability of the corticospinal tract, which constitutes the "common final pathway," while changes in SP duration reflect intracortical inhibitory influences projecting on this pathway. TMS can thus be used to provide online measures of response implementation to investigate the level of

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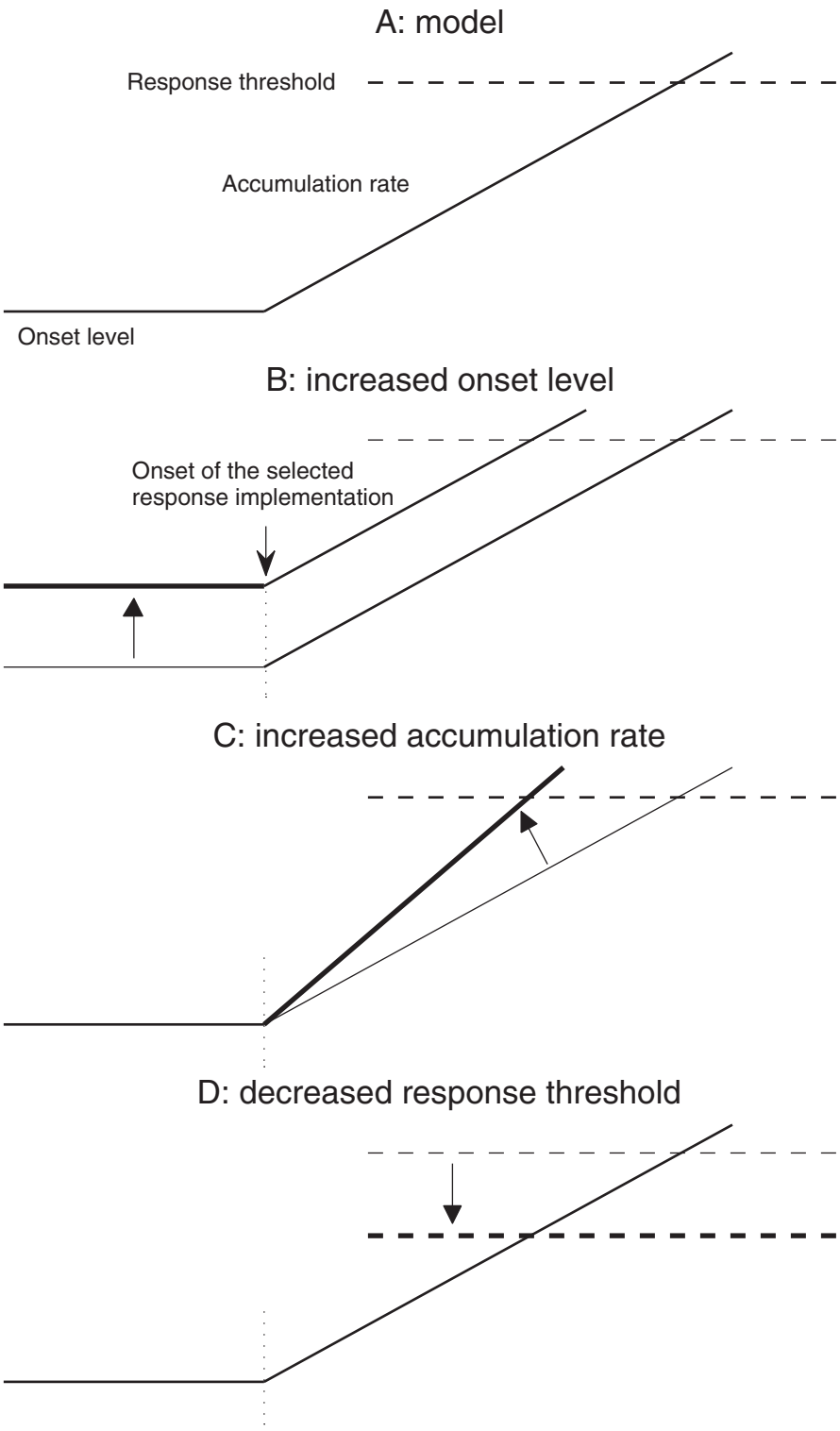

Figure 1. A: Decision-making models assuming that evidence favoring one alternative is integrated over time until a threshold level corresponding to the initiation of the selected response. The main relevant parameters are onset level of information accumulation (horizontal solid line), accumulation rate (oblique line), and response threshold (horizontal dashed line). The three hypotheses relative to the effect of temporal preparation on reaction time; arrows indicate which parameter is affected according to each hypothesis. In all instances, the response threshold is reached faster when participants are optimally prepared (thick lines) than when they were not optimally prepared (thin lines). B: Increased onset level of information accumulation reflected by reduced silent period (SP) duration or increased motor evoked potential (MEP) amplitude before response implementation. C: Increased accumulation rate reflected by reduced SP duration or increased MEP amplitude during response implementation. D: Decreased response threshold reflected by increased SP duration or decreased MEP amplitude prior to response execution (see text for details).

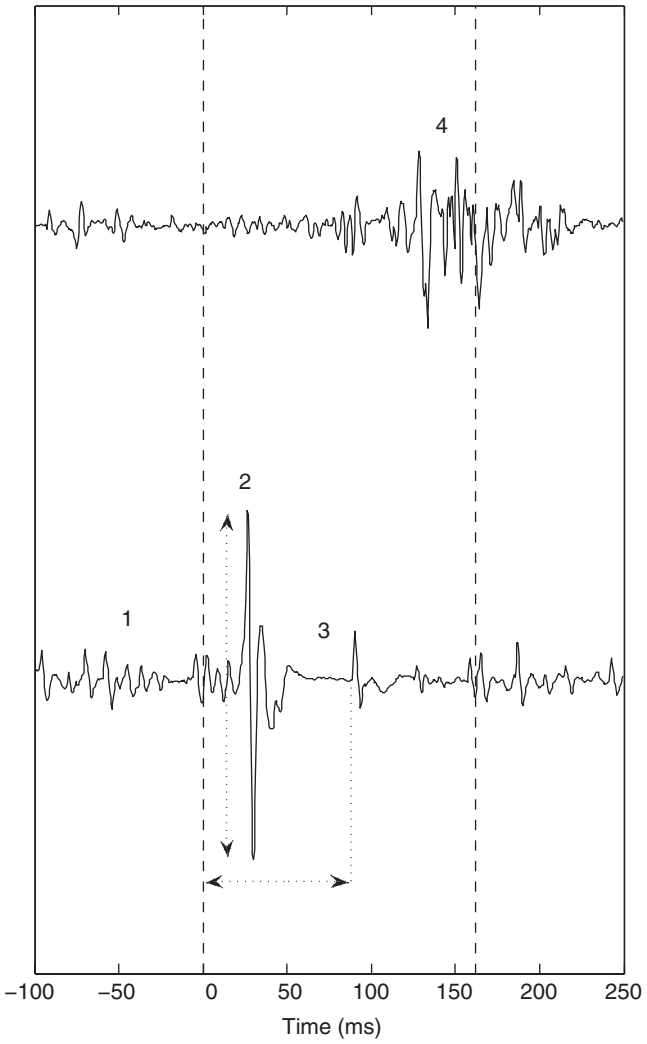

Figure 2. Example of a trial with transcranial magnetic stimulation (TMS) in the present study. The upper trace represents the EMG activity of the left *flexor pollicis brevis* (FPB) muscle and the lower trace the EMG activity of the right (stimulated) FPB muscle. The left dashed line (0 of time) represents the imperative stimulus onset at which the TMS was delivered in this trial, and the right dashed line represents the mechanical response. (1) Tonic EMG activity before the TMS reflecting the preactivation of the muscles. (2) Motor evoked potential (MEP) following the TMS, visible on the right trace only since the TMS coil is located over the left primary motor cortex; the vertical arrows indicate the MEP amplitude. (3) Silent period (SP) following the MEP; the horizontal arrows indicate the SP duration. (4) EMG burst involved in the voluntary motor response.

excitability of both the motor cortex and the corticospinal pathway through SP duration and MEP amplitude measures, respectively (see Figure 2).

During constant short foreperiods allowing optimal preparation (termed "optimal" foreperiods in what follows; see, e.g., Boons & Bertelson, 1961), the MEP amplitude was found to decrease, revealing a reduction of corticospinal excitability (Hasbroucq, Kaneko, Akamatsu, & Possamaï, 1997; Touge, Taylor, & Rothwell, 1998) that occurs only when the agonist in which the MEP is elicited is a possible response (Duque, Lew, Mazzocchio, Olivier, & Ivry, 2010). In addition, we showed that for optimal foreperiods, SP duration shortens as time elapses, which provides evidence for an increase of cortical excitability (Davranche et al., 2007). This notion was confirmed by paired-pulse TMS experiments showing that the amplitude of the conditioned MEPs expressed relative to the test MEPs (3-ms interstimulus interval [ISI]) increases during foreperiods of both simple (Sinclair & Hammond, 2008, 2009) and choice RT tasks (Duque & Ivry, 2009; Tandonnet et al., 2010), providing evidence that short interval intracortical inhibition is released during the foreperiod. Temporal preparation seems thus to be implemented through the joint inhibition of excitatory and inhibitory projections onto the corticospinal pathway.

By stimulating the motor cortices controlling both the required and nonrequired responses at different times during the RT interval, different authors have reported a progressive, nonspecific increase in MEP amplitude (Burle, Bonnet, Vidal, Possamaï, & Hasbroucq, 2002; McMillan, Ivry, & Byblow, 2006; Tandonnet, Garry, & Summers, 2011). Thereafter, the MEP elicited by the motor cortex controlling the required response increases more than the MEP elicited by stimulation of the motor cortex controlling the nonrequired response (Koch et al., 2006; Leocani, Cohen, Wassermann, Ikoma, & Hallett, 2000; Tandonnet et al., 2011). In other words, after an initial nonspecific phase, the activation of the corticospinal tract becomes specific and directly reflects the implementation of the required response. In addition, the duration of the SP evoked by sTMS of the motor cortex controlling the required response progressively decreases before EMG onset, while symmetrically the duration of the SP evoked by stimulation of the motor cortex controlling the nonrequired response increases (Burle et al., 2002). These results indicate that the cortical inhibition exerted on the corticospinal tract involved in the required response is removed during RT, while the cortical inhibition exerted on the corticospinal neurons involved in the nonrequired response is increased (van den Wildenberg et al., 2010). In other words, the involved motor cortex becomes progressively more activated, while symmetrically the noninvolved motor cortex becomes more inhibited.

Here, we investigated the effect of temporal preparation on the dynamics of response implementation. Our objective was to determine whether temporal preparation affects the onset level of information accumulation, the accumulation rate, or the response threshold level. In order to put these hypotheses to test, we contrasted an optimal (500 ms) and a suboptimal (2500 ms) blocked foreperiod condition in a between-hand choice RT task. Response implementation was assessed at the motor cortex level through the evolution of SP duration and on the final motor pathway through changes in MEP amplitude. First, we assumed that the onset of the selected response implementation is indexed by the first significant dissociation between the responding and the nonresponding hands on SP and MEP measures, as reported in previous studies (e.g., Burle et al., 2002; Koch et al., 2006; Leocani et al., 2000; Tandonnet et al., 2011). Second, we assumed that (a) the onset level of information accumulation is indexed by the level of motor cortex excitability before the selected response is implemented; (b) the rate of information accumulation is indexed by the rate of increased motor cortex excitability after the selected response is implemented; and (c) the response threshold level is indexed by the level of motor cortex excitability just prior to response execution.

The three hypotheses are presented in Figure 1. We reasoned that an increased onset level of information accumulation should lead to an increased motor cortex excitability before the selected response is implemented. This hypothesis predicts a reduction of SP duration or an increase of MEP amplitude more pronounced for the optimal foreperiod condition before the dissociation between the responding and the nonresponding conditions on these meas-

ures. In contrast, an increased accumulation rate predicts that motor cortex excitability should be unaffected before the selected response implementation and increased after it. This second hypothesis predicts a reduction of SP duration or an increase of MEP amplitude more pronounced for the optimal foreperiod condition after the SP/MEP dissociation. The last hypothesis relative to the decreased response threshold level predicts that motor cortex excitability should be unaffected before and just after the selected response implementation but lower just prior to response execution. This third hypothesis predicts a reduction of SP duration or an increase of MEP amplitude less pronounced for the optimal foreperiod condition for the last TMS time prior to EMG activation.

Methods

Participants

Eight healthy participants (three women and five men, mean age: 27 years, age range: 20–32 years) with self-reported right handedness and normal or corrected-to-normal vision volunteered for the experiment. Informed written consent was obtained according to the Declaration of Helsinki, and the local ethics committee approved the experiment.

Behavioral Set-Up

Participants were seated in a comfortable chair in a darkened room with supports for forehands and hands. They gripped two vertical cylinders fixed 12 cm apart on a pullout table. The distal phalanx of each thumb rested on a force sensor fixed on the top of the cylinder. Participants faced a black panel at a distance at eye level of 1 m. Three horizontal rows of two light-emitting diodes (LEDs), one central green row and two outer red rows, were positioned at the center of the panel with a distance of 2 cm between rows and 4 cm within rows. The two central LEDs displayed the response signal. The two upper and the two lower LEDs gave online feedback about the force exerted on the left and right sensors. The lower LEDs lit up when the force exerted by the thumb on the sensor was in the correct range of force to initiate the trial (from 10 to 20 N) and the upper LEDs lit up when the force was too high (>20 N). The lighting of a blue LED at the top of the panel indicated to participants that they could initiate the trial by exerting isometric presses on the sensors. This self-initiation procedure was intended to generate a background EMG activity necessary to observe a SP.

Trial Events

Participants initiated each trial by exerting an isometric press on both sensors. Participants had to attain the correct range of force and then to maintain it during 3 s. The duration of the isometric press was similar for both foreperiod durations (500 and 2500 ms). If the force was below or over the allowed window before the end of the 3-s period, participants had to initiate another isometric press with the correct range of force for a 3-s period. The foreperiod duration was varied between blocks. An auditory warning signal (1000 Hz, 75 dB, 50 ms in duration) was presented within the 3-s period at either 500 ms (optimal foreperiod condition) or 2500 ms (suboptimal foreperiod condition) before the imperative stimulus (i.e., corresponding to 2500 ms and 500 ms after the correct range of force is reached, respectively). This procedure ensured that the duration of isometric contraction was identical across foreperiod conditions. At the end of the 3-s period, one of the two possible imperative stimuli (left or right red middle row LEDs) lit up. Participants were instructed to perform as quickly as possible the isometric press spatially compatible with the location of the imperative stimulus (e.g., left press for a stimulus presented on the left). An auditory feedback was emitted when the first isometric press exceeding 20 N was on the correct side during the time period allowed to respond (1 s). The display was switched off with the response or at the end of the responding period. To initiate a new trial, participants had to wait a minimal intertrial interval of 1500 ms.

Design

Participants performed first a training session without TMS in order to reach a stable level of RT performance. They then performed two sessions with TMS, an experimental and a sham session; each ran on a different day and in a counterbalanced order between participants. In each session, the two foreperiod conditions alternated every block of trials in a counterbalanced order between participants. Each block comprised 96 trials in which each imperative stimulus (left/right) occurred 48 times in a pseudorandom sequence.

The training session was considered as completed when (a) error rate was below 5%, and (b) coefficient of variation (standard deviation divided by the mean) of RT was at most 0.15 during two consecutive blocks of trials. During this training session, EMG was recorded in order to estimate the voluntary EMG onset of the individual distributions (e.g., Burle et al., 2002). To this end, the single-trial EMG activity was displayed on a computer screen aligned to the onset of the imperative stimulus, and the onset of the change in activity was determined visually and marked with the computer mouse. Although laborious, this method was preferred to an automated one because it allows precise detection provided that the EMG is recorded at a high sampling rate with an anti-aliasing filter (Staude, Flachenecker, Daumer, & Wolf, 2001; Van Boxtel, Geraats, Van den Berg-Lenssen, & Brunia, 1993).

In the experimental session (ten blocks), single-pulse TMS was delivered over the left primary motor cortex and in the sham session (six blocks), TMS was delivered over the parietal cortex. In both sessions, TMS was delivered during the RT at seven possible times individually adjusted from EMG onset of the responses performed with the right hand in the last two blocks of the training session (see, e.g., Burle et al., 2002, Figure 2, p. 211). Within a block, 12 no-TMS trials and 12 TMS trials for each TMS time occurred in a pseudorandom sequence. For the optimal foreperiod duration, the first TMS time was at the imperative stimulus onset and the six following times were equally spread between 60 ms after the imperative stimulus onset and the first decile of each individual distribution. The last five TMS times for the optimal foreperiod were on average 70 ms (standard deviation = 3), 79 ms (SD = 5), 89 ms (SD = 8), 98 ms (SD = 11), and 107 ms (SD = 13). For the suboptimal foreperiod, the first six TMS times were the same as for the optimal foreperiod and differed only for the last TMS time that was set according to the first decile of each individual distribution for the suboptimal foreperiod (on average at 125 ms, SD = 10).

Transcranial Magnetic Stimulation

TMS was delivered using a Magstim 200 (Magstim, Whitland, UK) connected to a figure-of-eight coil (double 70 mm-diameter coil, maximum output intensity: 2.2 T, stimulation duration < 1 ms).

During the experimental session, the coil was placed tangentially on the head over the hand area of the left motor cortex. To this end, the coil was initially positioned 6 cm to the left of the vertex (C3 location in the 10/20 system) and then slightly moved in antero-posterior and coronal directions until the lowest threshold spot for activating the right *flexor pollicis brevis* (FPB) muscle was reached. During the sham session, the coil was positioned 6 cm posterior of the vertex (Pz location in the 10/20 system). The coil was held in position by a clamp mounted on a mechanical arm with six degrees of freedom and bolted on the back of the chair. A vacuum-controlled head support assured a light and comfortable maintaining of the head of the participants (Butterfly head support 155, Burnett Body Supports).

Computer-piloted series of adjustment trials were performed to adjust the TMS intensity on an individual basis. To this end, participants were asked to maintain a constant pressure (between 10 and 20 N) with their thumbs on the force sensors during the delivering of 20 single-pulse TMS in a pseudorandom temporal sequence. The EMG signal was then averaged time-locked to the TMS delivery and displayed on the computer screen to be visually examined. The TMS intensity was set at 5% above the minimal TMS intensity needed to evoke a MEP of about 100 μV peak-to-peak amplitude (based on the averaging of the 20 trials). Mean TMS intensity corresponded to 34% ($SD = 4$) of the maximal stimulator output.

EMG and Force Recordings

EMG activity was recorded from paired 6 mm-diameter Ag/AgCl surface electrodes glued 2 cm apart on the thenar eminence over the FPB muscle. The EMG signal was amplified with a gain of 2000, filtered using a 50 Hz notch filter, 10 Hz high-pass (12 dB/octave) and 1 kHz low-pass (24 dB/octave) filters (P511, Grass Instruments, West Warwick, RI), and digitized online at a sampling rate of 2 kHz. The force signal was recorded from force sensors (Entran, Measurement Specialties, Fremont, CA) and digitized online at 2 kHz.

Signal Processing

The RT was measured between the imperative stimulus onset and the mechanical response defined as a press stronger than 20 N on one of the force sensors. In order to measure the MEP amplitude, the EMG signal recorded during the experimental session was first averaged time-locked to the TMS onset, and the averaged (nonrectified) MEP onset and offset were scored to define an individual "analysis" window. The window was on average from 24 ms ($SD = 1$) to 39 ms ($SD = 4$) after TMS onset. The peak-to-peak amplitude of the MEPs in the right FPB muscle was measured within the individual "analysis" window for each trial (i.e., for both the responses contralateral and ipsilateral to the stimulated cortex), and the mean was computed for each experimental condition. The SP duration was scored trial by trial based on visual inspection. To this end, each trial was displayed aligned with TMS onset (so that the experimenter was unaware of TMS onset time relative to stimulus and RT), and the experimenter marked with the computer mouse the SP duration from TMS onset to the return of the uninterrupted tonic EMG activity (as illustrated in Figure 2). Trials with EMG burst before the MEP were discarded. The mean overall percentage of rejected trials for the MEP computation was 12% ($SD = 5$). For the SP analysis, trials were excluded when the end of the SP was either interrupted by the voluntary EMG burst or obscured by the loss of EMG due to muscle relaxation. The mean overall percentage of rejected trials for the SP analysis was 47% ($SD = 14$). As the last two TMS intervals led to too many rejected trials (57%, $SD = 20$, and 66%, $SD = 18$), they have not been included in the analysis. To minimize the influence of extreme values within participants, the median of SP durations was individually computed for each experimental condition. Because of the large variability between participants (i.e., absolute values of MEP amplitudes and SP durations may considerably differ from one participant to another), MEP amplitudes and SP durations were converted into z scores before being submitted to statistical analyses (Burle et al., 2002; Davranche et al., 2007; Van Elswijk, Kleine, Overeem, & Stegeman, 2007). This was done in the following way: for each participant, the mean and standard deviation were computed for all experimental conditions (i.e., foreperiod duration, responding hand, and time of TMS delivery). The individual value of each experimental condition was subtracted by the mean and then divided by the standard deviation. This computation gives the same weight to the variances of the individual differences between experimental conditions whatever the absolute mean values.

Statistical Analysis

The mean RT for the no-TMS trials were submitted to univariate repeated measures analysis of variance (ANOVA) involving two within-subject factors: session (experimental, sham) and foreperiod duration (short, long). Note that in the following we will use the terms responding and nonresponding as shorthand for the cortex contralateral to the muscle involved in the response and the cortex ipsilateral to the muscle involved in the response, respectively. The MEP amplitudes (z scores) were submitted to univariate repeated measures ANOVA involving three within-subject factors: foreperiod duration (short, long), hand (responding, nonresponding), and TMS time (7 times). The same design was used for SP, except that only 5 TMS times were used. Huynh-Feldt correction was used for univariate repeated measures ANOVA tests involving more than one degree of freedom, in which case the uncorrected degrees of freedom, the corrected p value, and the ε value were reported. Newman-Keuls was used for *post hoc* tests.

Results

Behavioral Results

The behavioral effect of temporal preparation was confirmed: RT was shorter for the optimal (239 ms, $SD = 26$) than for the suboptimal foreperiod (271 ms, $SD = 32$, $F(1,7) = 31.97$, $p < .01$). This result was similar for both the TMS and the sham sessions, and there was no interaction between foreperiod duration and session (Fs$(1,7) < 1$). The overall error percentage including side errors, anticipations (RTs less than 100 ms), and omission errors was 0.4% ($SD = 0.5$); this was judged too low to warrant statistical analysis. This low error rate pattern excludes that speed–accuracy tradeoffs can account for the behavioral effect.

Motor Evoked Potential

The mean amplitude of the raw MEP was 1.1 mV ($SD = 1.0$). The MEP amplitudes (z scores) are presented in Figure 3. Inspection of the figure suggests two successive phases in the time-course of corticospinal excitability variations during the RT interval: an initial response-aspecific phase up to approximately 70 ms for the

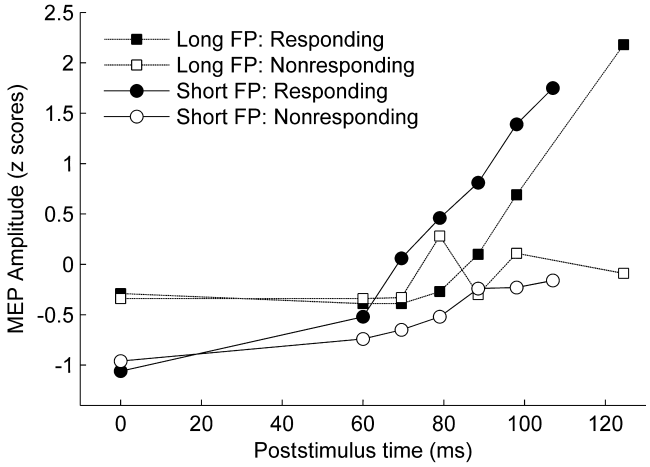

Figure 3. Motor evoked potential (MEP) amplitude (*z*-scores) as a function of poststimulus time (ms) for optimal (500 ms; solid line; dots) and suboptimal (2500 ms; dotted line; squares) foreperiods. Filled symbols correspond to the responding condition and empty dots to the nonresponding condition. Initial response-aspecific activation: in the first phase, the MEP deficit at stimulus presentation for the optimal foreperiod was compensated whatever the forthcoming response, suggesting a removal of preparatory corticospinal suppression. Later response-specific modulations: in the second phase, the MEP dissociation for responding and nonresponding occurred earlier for the optimal foreperiod, suggesting a faster integration of the response selection-related inputs to the corticospinal pathway.

optimal foreperiod followed by a response-specific phase. The response-aspecific increase of MEP amplitude following stimulus appears to be more pronounced for the optimal than for the suboptimal foreperiod. Figure 3 also suggests that the MEPs for the responding and the nonresponding hands differentiated sooner for the optimal than for the suboptimal foreperiod.

Statistical analysis confirmed this pattern. The MEP was larger for responding than for nonresponding ($F(1,7) = 137.44$, $p < .01$), and increased during the RT interval ($F(6,42) = 18.63$, $p < .01$, $\varepsilon = 1.00$). This increase was more pronounced for responding than for nonresponding, as revealed by an interaction between responding condition and TMS time ($F(6,42) = 10.69$, $p < .01$, $\varepsilon = .69$). The foreperiod duration influenced both the difference between responding and nonresponding ($F(1,7) = 8.01$, $p < .05$; no main effect of foreperiod duration, $F(1,7) < 1$) and the dynamics of the MEP increase (trend to an interaction between foreperiod duration and TMS time, $F(6,42) = 2.13$, $p = .09$, $\varepsilon = .82$). Moreover, this effect of foreperiod duration on the MEP dynamics depended on the hand involved in the response (interaction between foreperiod duration, TMS time, and responding condition, $F(6,42) = 4.31$, $p < .01$, $\varepsilon = .62$). Planned comparisons showed that the foreperiod affected the MEP dynamics for responding ($p < .01$) but not for nonresponding ($p = .23$). For responding, the MEP increase was linear for the optimal foreperiod ($p < .01$), and both linear and quadratic components were significant for the suboptimal foreperiod ($ps < .01$). For nonresponding, the MEP increase was linear ($p < .05$). *Post hoc* tests further showed that for the optimal foreperiod the MEP increase from stimulus onset was reliable from 70 ms poststimulus (for both responding and nonresponding, $ps < .01$), but for the suboptimal foreperiod such MEP increase during RT was reliable only from 98 ms (for responding only, $ps < .01$). When contrasting the two foreperiods, *post hoc* tests indicated that the MEP for responding was larger for the optimal than for the suboptimal foreperiod at 89 ms and 98 ms ($ps < .05$; the trend was in the opposite direction at 107 ms, $p = .07$). The above-reported interaction between foreperiod duration, TMS time, and responding condition also showed that the dissociation between responding and nonresponding occurred earlier for the optimal than for the suboptimal foreperiod. *Post hoc* tests revealed that this difference was significant at 79 ms for the optimal foreperiod ($p < .05$) and at 107 ms for the suboptimal foreperiod ($p < .01$; trend at 98 ms, $p = .07$). *Post hoc* tests independent of the responding hand showed that the MEP was smaller for the short than for the suboptimal foreperiod at stimulus onset ($p < .05$).

Silent Period Duration

The mean duration of the raw SP was 81 ms ($SD = 13$). The SP durations (*z* scores) are presented in Figure 4. This figure shows that SP duration was shorter for the optimal than for the suboptimal foreperiod during the RT interval, indicating a release of cortical inhibition when temporal preparation is better. Statistical analysis confirmed this pattern. The SP duration was indeed shorter for optimal than for suboptimal foreperiod ($F(1,7) = 6.79$, $p < .05$) during the RT interval. Relative to the dynamics, SP duration was on average shorter for responding than for nonresponding ($F(1,7) = 7.82$, $p < .05$) and was reduced during the RT interval ($F(4,28) = 6.66$, $p < .05$, $\varepsilon = .48$); this reduction was more pronounced for responding than for nonresponding ($F(4,28) = 14.65$, $p < .01$, $\varepsilon = 1.00$). Planned comparisons indicated that for responding both linear and quadratic components were significant ($ps < .05$) and for nonresponding the quadratic component was significant ($p < .05$). These comparisons suggest that, after an initial reduction, the SP duration was further reduced for responding but lengthened for nonresponding. Indeed, *post hoc* tests showed a dissociation between responding and nonresponding that was significant from 79 ms poststimulus ($ps < .01$); they further revealed a significant reduction for responding from stimulus onset to 89 ms poststimulus ($ps < .01$) and a significant lengthening for nonresponding between 70 ms and 89 ms poststimulus ($p < .05$). The foreperiod duration did not influence the dynamics

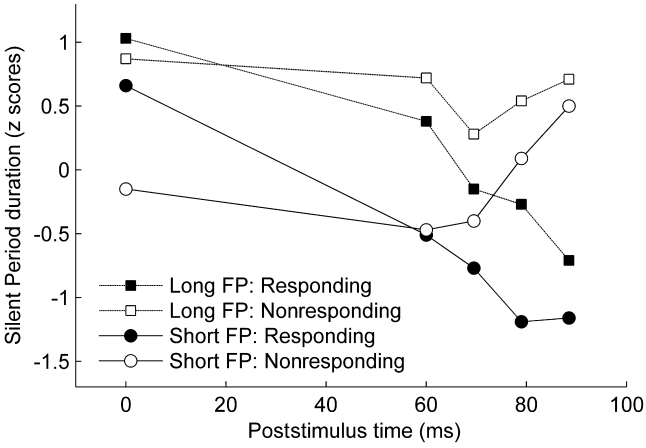

Figure 4. Silent period (SP) duration (*z*-scores) as a function of poststimulus time (ms) for optimal (500 ms; solid line; dots) and suboptimal (2500 ms; dotted line; squares) foreperiods. Filled symbols correspond to the responding condition and empty dots to the nonresponding condition. The silent period duration was shorter for the optimal foreperiod, suggesting a more pronounced release of cortical inhibition.

($F(4,28) = 1.61$, $p = .20$, $\varepsilon = 1.00$) and the hand involved in the response ($F(1,7) < 1$; the three-way interaction between these factors was not significant, $F(4,28) < 1$). *Post hoc* tests further showed that the difference in SP duration for the optimal and the suboptimal foreperiods was significant from stimulus onset to 79 ms poststimulus ($ps < .05$), thus already evident prior to the dissociation between responding and nonresponding.

Discussion

We addressed whether temporal preparation affects the onset level of information accumulation, the accumulation rate, or the response threshold level on the basis of variations in both SP and MEP induced by sTMS. We assessed response implementation at the motor cortex level through the evolution of SP duration and on the final motor pathway through changes in MEP amplitude. First, we assumed that the onset of the selected response implementation is indexed by the first significant dissociation between the responding and the nonresponding hands on SP and MEP measures, as reported in previous studies (e.g., Burle et al., 2002; Koch et al., 2006; Leocani et al., 2000; Tandonnet et al., 2011). Second, we assumed that (a) the onset level of information accumulation is indexed by the level of motor cortex excitability before the selected response is implemented; (b) the rate of information accumulation is indexed by the rate of increased motor cortex excitability after the selected response is implemented; and (c) the response threshold level is indexed by the level of motor cortex excitability just prior to response execution. Changes in SP duration showed that the level of response activation assessed within the motor cortex was increased prior to the selected response implementation when temporal preparation is optimal. Such an early cortical activation favors an effect of temporal preparation on the onset level of accumulation. Moreover, the earlier activation of the final motor pathway for the selected response, as evidenced on the MEP modulations, may be the consequence of this early activation. In what follows, we will describe and comment on the dynamics of response implementation during the RT interval and its modulation by temporal preparation during two successive phases: (1) early response-aspecific activation following stimulus presentation; and (2) later response-specific modulations.

Early Response-Aspecific Activation Following Stimulus Presentation

Following stimulus presentation, SP duration was initially reduced whatever the forthcoming response, replicating previous results (Burle et al., 2002). This modulation indicates a reduction of intracortical inhibition during RT (e.g., Terao & Ugawa, 2002). Moreover, in the present study, SP duration was shorter for the optimal than for the suboptimal foreperiod, revealing that this cortical activation was more pronounced for the foreperiod that led to the shortest RT. This is in line with recent studies using paired-pulse TMS paradigms (3-ms ISI), showing that conditioned MEPs relative to test MEPs increased during the foreperiod, indicating release of short intracortical inhibition (Duque & Ivry, 2009; Sinclair & Hammond, 2008, 2009; Tandonnet et al., 2010). Furthermore, a larger reduction of SP duration was found during the optimal compared to the suboptimal foreperiod, suggesting that temporal preparation involves a more pronounced overall activation of the motor cortex during the optimal foreperiod (Davranche et al., 2007). The present findings extend previous ones by showing that the reduction of cortical inhibition initiated during the foreperiod kept on going after stimulus onset. Cortical inhibition is thought to be mediated by GABA-ergic neurotransmitters: short intracortical inhibition obtained with paired-pulse TMS paradigms through $GABA_A$ receptors (Ziemann, Lönnecker, Steinhoff, & Paulus, 1996) and intracortical inhibition assessed by silent period duration through $GABA_B$ receptors (Siebner, Dressnandt, Auer, & Conrad, 1998; Werhahn, Kunesch, Noachtar, Benecke, & Classen, 1999; see Ziemann, 2004, for a review). Temporal preparation may thus result in an overall activation of the motor cortex reflected by a reduction of cortical inhibition mediated through $GABA_B$ receptors.

The MEP amplitude was found to increase following stimulus presentation, replicating previous studies (e.g., Burle et al., 2002; McMillan et al., 2006; Tandonnet et al., 2011). As this MEP increase occurred whatever the forthcoming response, it reflects response-aspecific inputs to the corticospinal pathway. This early aspecific modulation is compatible with the notion that, in decision tasks, potential responses can be activated in the motor system before the selection between them is completed (Cisek & Kalaska, 2005). However, as corticospinal excitability is reduced during the foreperiod (Hasbroucq et al., 1997; Touge et al., 1998), this corticospinal activation may also reflect a compensatory mechanism during RT, as proposed in previous studies (e.g., McMillan et al., 2006). Indeed, in the present study, the early response-aspecific MEP increase was found to be more pronounced for the optimal foreperiod, which likely reflects the removal of the corticospinal suppression set up during the foreperiod. The MEP decrease during the foreperiod may indeed reflect inhibition at the spinal level as proposed in previous studies (Duque et al., 2010; McMillan et al., 2006), suggesting that such a removal of corticospinal suppression during RT involves spinal mechanisms. In line with this notion, previous studies showed that spinal modulations occur during foreperiod (Prut & Fetz, 1999), and that monosynaptic reflexes are reduced during the foreperiod (e.g., Brunia, 1984; Hasbroucq, Kaneko, Akamatsu, & Possamaï, 1999). A single motor unit study in humans further showed that the mean interspike interval was lengthened and its variability was decreased during the foreperiod (Duclos, Schmied, Burle, Burnet, & Rossi-Durand, 2008), suggesting that spinal inhibitory mechanisms are implemented during foreperiod. However, these motoneuronal modulations were more pronounced for the suboptimal than for the optimal foreperiod. In contrast, the MEP modulation at stimulus occurrence in both the present study and in previous ones (e.g., Hasbroucq et al., 1997) is associated with the optimal foreperiod that leads to the shorter RT performance. Hence, the spinal mechanisms discussed by Duclos et al. (2008) cannot account for the preparatory MEP modulations.

This early activation during RT evidenced at both cortical and corticospinal levels may reflect a general mechanism involved in decision tasks that contribute to activating the potential responses before response selection (see Cisek & Kalaska, 2010, for a review). At the corticospinal level, this early activation increase may also reflect a compensatory mechanism from preparatory suppression. The influence of foreperiod duration on the response-aspecific MEP modulations then likely reflects a return to the onset level prior to the preparatory suppression. Temporal preparation may also enhance the early activation evidenced at the cortical level. Indeed, foreperiod duration does not influence the dynamics of the early cortical activation but only its overall amplitude level. Such a modulation occurring prior to the first evidence of response selection is not predicted by the accumulation rate or the response threshold level hypotheses, rather it favors an effect of temporal preparation on the onset level of accumulation.

Later Response-Specific Modulations During RT

Later on during RT, the SP duration was reduced for the responding hand and lengthened for the nonresponding one (Burle et al., 2002). The SP dissociation for the responding and the nonresponding hands occurred at a comparable time for both foreperiods, providing no evidence that temporal preparation modulates the latency of the response-specific inputs to the motor cortex. It is thus possible that response-specific inputs reach the motor cortex at the same time for both foreperiods but are integrated faster within the motor cortex for optimal foreperiods due to the prior overall activation. Such an increase of the efficiency of the motor system through combined release of cortical inhibition within the motor cortex and inhibition of its corticospinal output exemplifies a role of intracortical (release of) inhibition in modulating the sensitivity of the cortical structures to the response-specific cortical inputs. Previous studies emphasized the role of intracortical circuits in movement initiation (e.g., Floeter & Rothwell, 1999), based notably on the assumption that a release of intracortical inhibition is required for response implementation (Reynolds & Ashby, 1999; but see Tandonnet et al., 2011). Here, we found a more pronounced reduced SP duration for the optimal foreperiod before the first significant dissociation between the responding and the nonresponding hands. These findings extend previous ones by suggesting that temporal preparation involves a more pronounced release of intracortical inhibition already prior to the implementation of the selected response. Moreover, the dynamics of the SP modulations during RT were comparable for both foreperiods. Thus, these results provided no evidence to support the accumulation rate or the response threshold level hypotheses; instead, they are compatible with an effect of temporal preparation restricted to the onset level of accumulation.

At the corticospinal level, the MEP amplitude increased more for the responding hand than for the nonresponding one, replicating previous findings (Koch et al., 2006; Leocani et al., 2000; Tandonnet et al., 2011). As stated in the introduction, this MEP dissociation provides evidence that the excitability of the final motor pathway increased specifically for the selected response, reflecting response implementation. The present results revealed that the MEP dissociation occurred earlier for the optimal than for the suboptimal foreperiod, thereby supporting the notion that the selected response is implemented faster when participants are optimally prepared. These specific corticospinal modulations may be due to changes in functional connectivity between the dorsal premotor cortex and the motor cortex, as shown in a paired-pulse TMS study (Koch et al., 2006). Interestingly, these connectivity changes have been found to be independent of intracortical circuits within the motor cortex (Koch et al., 2006). This leads to the speculation that the modulation of intracortical inhibition observed in the present study can operate in parallel with corticocortical interactions between the premotor and the motor cortex. As recently proposed (Tandonnet et al., 2010), a higher response-aspecific activation of the motor cortex during RT should lead to a faster implementation of the specific response called by the incoming stimulus. As discussed above, the SP shortening for the optimal foreperiod indicates an overall increase in excitability of the motor cortex during RT. Hence, if such cortical activation is responsible for the behavioral effect of temporal preparation, it should speed up the integration of the response-specific inputs within the motor cortex. The influence of this cortical activation should then be manifest on the time-course of the final motor pathway excitability, which was evidenced by the MEP modulations observed in the present study. The present findings suggest that early modulations within the motor cortex can account for the expedited response implementation, thereby providing support for the onset level hypothesis of the effect of temporal preparation.

Conclusion

The present study showed a reduced SP duration prior to the first evidence of response selection for the optimal foreperiod, providing evidence that temporal preparation involves an early cortical activation. The earlier MEP dissociation for the optimal foreperiod is compatible with the notion that the selected response is implemented faster when participants are better prepared, suggesting that the early cortical activation plays a role in the speeding up of the response implementation. We propose that the early activation at the motor cortex level reflects an increased efficiency of the motor system that effectively led to a faster implementation of the selected response. Such an activation may be implemented by an intracortical release of inhibition that modulates the sensitivity of the cortical structures to the response-specific cortical inputs. In the framework of accumulator models, such an early cortical activation is compatible only with an effect of temporal preparation on the onset level of information accumulation.

References

Bausenhart, K. M., Rolke, B., Seibold, V. C., & Ulrich, R. (2010). Temporal preparation influences the dynamics of information processing: Evidence for early onset of information accumulation. *Vision Research*, *50*, 1025–1034. doi: 10.1016/j.visres.2010.03.011

Boons, J. P., & Bertelson, P. (1961). Influence de l'incertitude temporelle sur le temps de réaction de choix. *L'année psychologique*, *61*, 361–376.

Brunia, C. H. (1984). Selective and aselective control of spinal motor structures during preparation for movement. In S. Kornblum & J. Requin (Eds.), *Preparatory states and processes* (pp. 285–302). Hillsdale, NJ: Erlbaum.

Burle, B., Bonnet, M., Vidal, F., Possamaï, C. A., & Hasbroucq, T. (2002). A transcranial magnetic stimulation study of information processing in the motor cortex: Relationship between the silent period and the reaction time delay. *Psychophysiology*, *39*, 207–217. doi: 10.1017.S0048577201392119

Cisek, P., & Kalaska, J. F. (2005). Neural correlates of reaching decisions in dorsal premotor cortex: Specification of multiple direction choices and final selection of action. *Neuron*, *45*, 801–814. doi: 10.1016/j.neuron.2005.01.027

Cisek, P., & Kalaska, J. F. (2010). Neural mechanisms for interacting with a world full of action choices. *The Annual Review of Neuroscience*, *33*, 269–298. doi: 10.1146/annurev.neuro.051508.135409

Davranche, K., Tandonnet, C., Burle, B., Meynier, C., Vidal, F., & Hasbroucq, T. (2007). The dual nature of time preparation: Neural activation and suppression revealed by transcranial magnetic stimulation of the motor cortex. *European Journal of Neuroscience. 25*, 3766–3774. doi: 10.1111/j.1460-9568.2007.05588.x

Duclos, Y., Schmied, A., Burle, B., Burnet, H., & Rossi-Durand, C. (2008). Anticipatory changes in human motoneuron discharge patterns during motor preparation. *The Journal of Physiology*, *586*, 1017–1028. doi: 10.1113/jphysiol.2007.145318

Duque, J., & Ivry, R. B. (2009). Role of corticospinal suppression during motor preparation. *Cerebral Cortex*, *19*, 2013–2024. doi: 10.1093/cercor/bhn230

Duque, J., Lew D., Mazzocchio, R., Olivier, E., & Ivry, R. B. (2010). Evidence for two concurrent inhibitory mechanisms during response preparation. *The Journal of Neuroscience*, *30*, 3793–3802. doi: 10.1523/jneurosci.5722-09.2010

Floeter, M. K., & Rothwell, J. C. (1999). Releasing the brakes before pressing the gas pedal. *Neurology*, *53*, 664–665.

Hasbroucq, T., Kaneko, H., Akamatsu, M., & Possamaï, C. (1997). Preparatory inhibition of cortico-spinal excitability: A transcranial magnetic stimulation study in man. *Cognitive Brain Research*, *5*, 185–192.

Hasbroucq, T., Kaneko, H., Akamatsu, M., & Possamaï, C. (1999). The time-course of preparatory spinal and cortico-spinal inhibition: An H-reflex and transcranial magnetic stimulation study in man. *Experimental Brain Research*, *124*, 33–41.

Koch, G., Franca, M., Fernandez Del Olmo, M., Cheeran, B., Milton, R., Alvarez Sauco, M., & Rothwell, J. C. (2006). Time course of functional connectivity between dorsal premotor and contralateral motor cortex during movement selection. *The Journal of Neuroscience*, *26*, 7452–7459. doi: 10.1523/jneurosci.1158-06.2006

Leocani, L., Cohen, L. G., Wassermann, E. M., Ikoma, K., & Hallett, M. (2000). Human corticospinal excitability evaluated with transcranial magnetic stimulation during different reaction time paradigms. *Brain*, *123*, 1161–1173.

McMillan, S., Ivry, R. B., & Byblow, W. D. (2006). Corticomotor excitability during a choice-hand reaction time task. *Experimental Brain Research*, *172*, 230–245. doi: 10.1007/s00221-005-0331-4

Ni, Z., Gunraj, C., & Chen, R. (2007). Short interval intracortical inhibition and facilitation during the silent period in human. *The Journal of Physiology. 583*, 971–982. doi: 10.1113/jphysiol.2007.135749

Prut, Y., & Fetz, E. E. (1999). Primate spinal interneurons show premovement instructed delay activity. *Nature*, *401*, 590–594.

Ratcliff, R., & Smith, P. L. (2004). A comparison of sequential sampling models for two-choice reaction time. *Psychological Review*, *111*, 333–367.

Reis, J., Swayne, O. B., Vandermeeren, Y., Camus, M., Dimyan, M. A., Harris-Love, M., . . . Cohen, L. G. (2008). Contribution of transcranial magnetic stimulation to the understanding of cortical mechanisms involved in motor control. *The Journal of Physiology*, *586*, 325–351. doi: 10.1113/jphysiol.2007.144824

Requin, J., Brener, J., & Ring, C. (1991). Preparation for action. In J. R. Jennings & M. G. H. Coles (Eds.), *Handbook of cognitive psychophysiology: Central and autonomic nervous system approaches* (pp. 357–448). Chichester, UK: Wiley.

Reynolds, C., & Ashby, P. (1999). Inhibition in the human motor cortex is reduced just before a voluntary contraction. *Neurology*, *53*, 730–735.

Ridding, M. C., & Rothwell, J. C. (2007). Is there a future for therapeutic use of transcranial magnetic stimulation? *Nature Review Neuroscience*, *8*, 559–567. doi: 10.1113/jphysiol.2007.144824

Schnitzler, A., & Benecke, R. (1994). The silent period after transcranial magnetic stimulation is of exclusive cortical origin: Evidence from isolated cortical ischemic lesions in man. *Neuroscience Letters*, *180*, 41–45.

Siebner, H. R., Dressnandt, J., Auer, C., & Conrad, B. (1998). Continuous intrathecal baclofen infusions induced a marked increase of the transcranially evoked silent period in a patient with generalized dystonia. *Muscle Nerve*, *21*, 1209–1212.

Sinclair, C., & Hammond, G. R. (2008). Reduced intracortical inhibition during the foreperiod of a warned reaction time task. *Experimental Brain Research*, *186*, 385–392. doi: 10.1007/s00221-007-1241-4

Sinclair, C., & Hammond, G. R. (2009). Excitatory and inhibitory processes in primary motor cortex during the foreperiod of a warned reaction time task are unrelated to response expectancy. *Experimental Brain Research*, *194*, 103–113. doi: 10.1007/s00221-008-1684-2

Staude, G., Flachenecker, C., Daumer, N., & Wolf, W. (2001). Onset detection and surface electromyographic signals: A systematic comparison of methods. *EURASIP Journal on Applied Signal Processing*, *2*, 67–81.

Tandonnet, C., Garry, M. I., & Summers, J. J. (2010). Cortical activation during temporal preparation assessed by transcranial magnetic stimulation. *Biological Psychology*, *85*, 481–486. doi: 10.1016/j.biopsycho.2010.08.016

Tandonnet, C., Garry, M. I., & Summers, J. J. (2011). Selective suppression of the incorrect response implementation in choice behavior assessed by transcranial magnetic stimulation. *Psychophysiology*, *48*, 462–469. doi: 10.1111/j.1469-8986.2010.01121.x

Terao, Y., & Ugawa, Y. (2002). Basic mechanisms of TMS. *Journal of Clinical Neurophysiology*, *19*, 322–343.

Touge, T., Taylor, J. L., & Rothwell, J. C. (1998). Reduced excitability of the cortico-spinal system during the warning period of a reaction time task. *Electroencephalography and Clinicial Neurophysiology*, *109*, 489–495.

Uncini, A., Treviso, M., Di Muzio, A., Simone, P., & Pullman, S. (1993). Physiological basis of voluntary activity inhibition induced by transcranial cortical stimulation. *Electroencephalography and Clinical Neurophysiology*, *89*, 211–220.

Van Boxtel, G. J., Geraats, L. H., Van den Berg-Lenssen, M. M., & Brunia, C. H. (1993). Detection of EMG onset in ERP research. *Psychophysiology*, *30*, 405–412.

van den Wildenberg, W. P. M., Burle, B., Vidal, F., van der Molen, M. W., Ridderinkhof, K. R., & Hasbroucq, T. (2010). Mechanisms and dynamics of cortical motor inhibition in the stop-signal paradigm: A TMS study. *Journal of Cognitive Neuroscience*, *22*, 225–239. doi: 10.1162/jocn.2009.21248

Van Elswijk, G., Kleine, B. U., Overeem, S., & Stegeman, D. F. (2007). Expectancy induces dynamic modulation of corticospinal excitability. *Journal of Cognitive Neuroscience*, *19*, 121–131. doi: 10.1162/jocn.2007.19.1.121

Werhahn, K. J., Kunesch, E., Noachtar, S., Benecke, R., & Classen, J. (1999). Differential effects on motorcortical inhibition induced by blockade of GABA uptake in humans. *The Journal of Physiology*, *517*, 591–597.

Woodrow, H. (1914). The measurement of attention. *Psychological Monographs*, *17*, 1–158.

Ziemann, U. (2004). TMS and drugs. *Clinical Neurophysiology*, *115*, 1717–1729.

Ziemann, U., Lönnecker, S., Steinhoff, B. J ., & Paulus, W. (1996). The effect of lorazepam on the motor cortical excitability in man. *Experimental Brain Research*, *109*, 127–135. doi: 10.1016/j.clinph.2004.03.006

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