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ORIGINAL ARTICLE

Investigating the effect of anticipating a startling acoustic stimulus on preparatory inhibition

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Summary
Objectives. — Motor-evoked potentials (MEPs) to transcranial magnetic stimulation (TMS) show a profound suppression when elicited during the instructed-delay of reaction time (RT) tasks. One predominant hypothesis is that this phenomenon, called ''preparatory inhibition'', reflects the operation of processes that suppress motor activity to withhold prepared (but delayed) responses, a form of impulse control. In addition, a startling acoustic stimulus (SAS) — a loud and narrow sound — can trigger the release of prepared responses in RT tasks. We predicted that, if such premature release is clearly forbidden, then anticipating a SAS during delay periods may be associated with increased preparatory inhibition for greater impulse control.
Methods. — Subjects performed a behavioural ($n=16$) and TMS ($n=11$) experiment. Both used a choice RT task that required subjects to choose a response based on a preparatory cue but to only release it after an imperative signal. SAS and TMS pulses were elicited at the end of the delay period and subjects were asked to do their best to only release their response after the imperative signal, even in the presence of SAS. SAS could be either rare or frequent, in separate blocks.
Results. — Consistent with the literature, SAS shortened RTs, especially when they occurred frequently. Moreover, MEPs were suppressed when subjects delayed prepared responses but this preparatory inhibition did not depend on whether SAS were frequent or rare.
Discussion. — The stronger RT shortening with frequent rather than rare SAS may be due to increased attention and/or reduced reactive inhibition to SAS, leaving preparatory inhibition unaffected.

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Introduction

Acting adequately in everyday life often requires the ability to inhibit prevailing tendencies that are not consistent with our internal goals or to suppress actions that are no longer appropriate [44,62]. When deficient, this capacity called response inhibition, can lead to improper behaviours, such as those seen in addiction and attention deficit hyperactivity disorders [2,54,61].

Response inhibition is commonly conceptualized as an executive function relying largely on the structural and functional integrity of the prefrontal cortex [3]. However, recent work using transcranial magnetic stimulation (TMS) has also implicated the motor system [32,65]. When applied over the primary motor cortex (M1), this non-invasive technique can elicit motor-evoked potentials (MEPs) in targeted contralateral hand or limb muscles; MEPs represent a valuable indicator of the excitability of the corticospinal (CS) motor output pathway at the time of stimulation, and their amplitude can be compared at various moments within a given condition and between different states [4,35,36].

Many TMS studies have evidenced a profound suppression of activity in the CS pathway in situations requiring abortion of a movement after a stop signal [32,64,65]. However, motor suppression is not solely present when one needs to abruptly stop an action but also during the preparation of a movement, a phenomenon referred to as preparatory inhibition [4,13,20,33,42,59]. Preparatory inhibition is particularly strong during instructed-delay reaction time (RT) tasks that require postponing a pre-cued response until a delayed imperative signal. In such conditions, one prominent hypothesis is that the motor suppression observed during the delay period assists impulse control, preventing the premature release of the prepared response [21,25].

Previous studies have shown that a loud (e.g., 124 dB) sound, called startling acoustic stimulus (SAS), can directly trigger the release of a prepared action when presented slightly before (−25 ms), simultaneously or after (+25 ms) the onset of an imperative signal in simple and choice RT tasks [27,46,48,49]. That is, the action is initiated much faster in trials including a SAS than in control trials; the RT shortening typically ranges from 46 to 62 ms [43] and can occur in parallel with a typical sequence of other events, including eye blink, neck flexion and facial grimacing, which together are referred to as a startle response [11,57].

In line with these observations, here we intended to characterize the impact of a SAS occurring before the imperative signal in an instructed-delay choice RT task, when the subject is actively withholding a prepared action. More critically, we aimed to assess whether anticipating the occurrence of a SAS can reduce its shortening impact on RTs (to avoid a penalty, see below), presumably due to the recruitment of impulse control processes that increase preparatory inhibition, in order to help prevent premature startle responses. To answer these questions, we performed both a behavioural ($n = 16$) and a TMS ($n = 11$) experiment. In both experiments, participants performed an instructed-delay choice RT task in two different block settings. In one type of block, the SAS were rare (referred to as ''Rare SAS''; RSAS context) whereas in the other block type they were frequent (''Frequent SAS''; FSAS context). The task was the same in both contexts and required the participants to perform a left or right index finger abduction movement according to a preparatory cue but to withhold their response until a delayed imperative signal. After that, they had to respond as fast as possible. The SAS was always elicited close to the end of the delay period and subjects were asked to do their best to only release their response after the imperative signal, even in the presence of a SAS. Critically, subjects were clearly told about the fact that the SAS may produce the release of their response prematurely and that they had to try to refrain from doing so (premature responses provided in less than 90 ms were penalized). Moreover, they knew whether the ongoing block would either involve a small amount (RSAS context) or a large amount of SAS (FSAS context), as this information was explicitly provided before the beginning of each block. Hence, based on the impulse control hypothesis, we predicted that in order to comply with the instruction to avoid responding prematurely, subjects would recruit more preparatory inhibition when they expected SAS to occur (FSAS) compared to when SAS were less likely (RSAS).

Materials and methods

Participants

A total of 27 subjects participated either in a behavioural ($n = 16$; 9 women; 21.9 ± 0.37 years old) or in a TMS experiment ($n = 11$; 7 women; 22 ± 0.75 years old). All were right-handed according to the Edinburgh Questionnaire [50]. None of them suffered from any neurological disorder or had a history of psychiatric illness, alcohol or drug abuse; none was taking drug treatment that could influence performance or neural activity. Participants were naive to the purpose of the study and were financially compensated. The protocol was approved by the institutional review board of the Université catholique de Louvain (Belgium) and required written informed consent.

Task

In both experiments, participants performed an instructed-delay choice RT task, which was implemented with Matlab 7.5 (Mathworks, Natick, Massachusetts, USA) using the Psychophysics Toolbox extensions [5,51]. The task consisted in a virtual rolling ball game previously used in other studies [53,54,59] (Fig. 1A). In this game, a ball and a goal appear on a computer screen and participants must ''shoot the ball into the goal'', by performing a movement with the left or right index finger. On each trial, the required response is indicated by the position of the ball, which serves as a preparatory cue: participants were instructed to prepare an abduction of the left index finger when the ball was presented on the left side of the screen, and an abduction of the right index finger when it appeared on the right. Subjects were told to release their prepared movement once a bridge was presented (imperative signal), allowing the ball to reach the goal. A score reflecting the subjects' performance was provided at the end of each trial. All objects were displayed on the computer screen with 3D perspective.

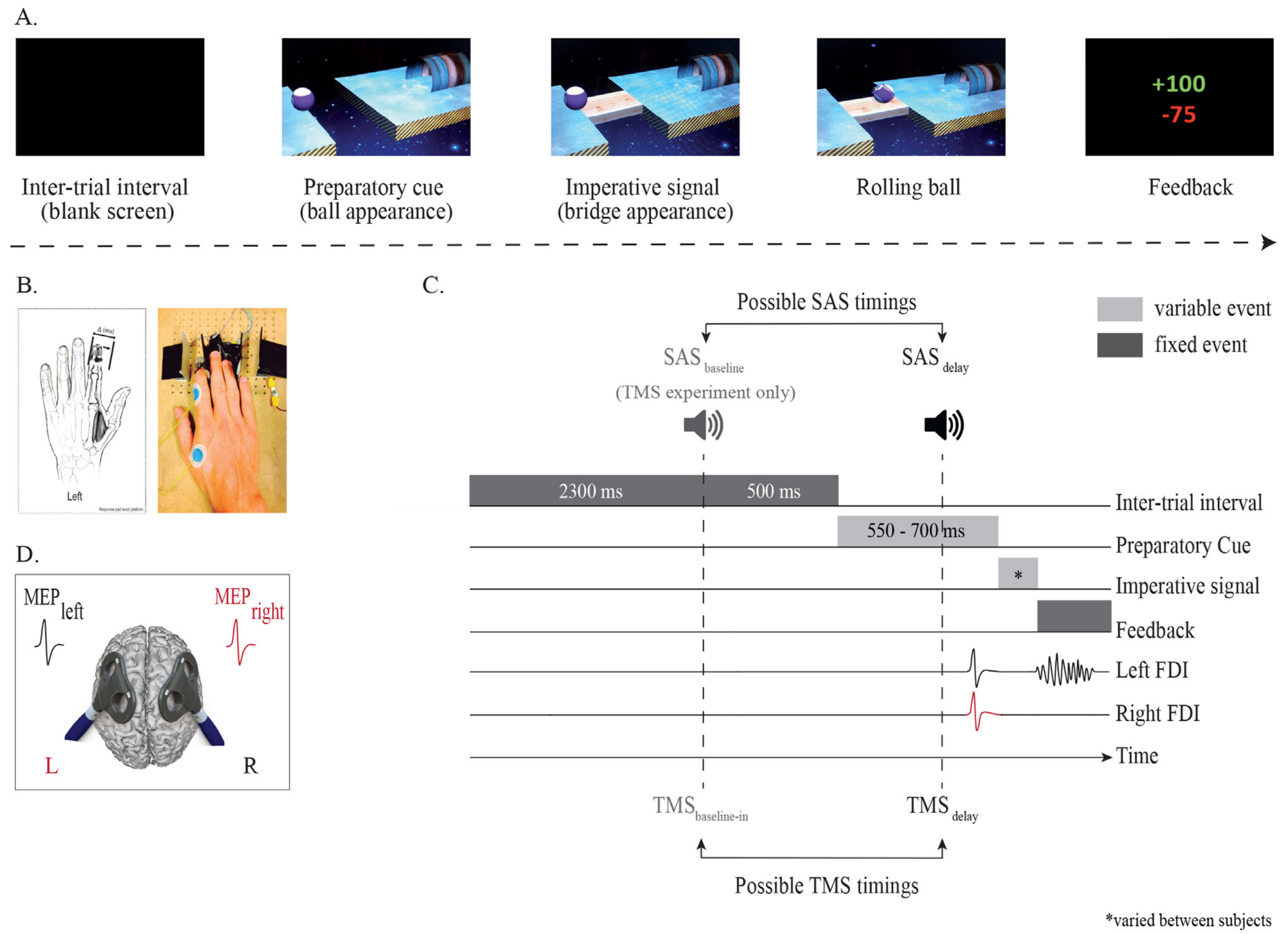

Figure 1 (A) Rolling Ball task. Participants were asked ''to shoot a ball in a goal'' on each trial. To do so, they had to provide a response with the left or right index finger according to the position of the ball (preparatory cue) which could appear either on the left or on the right side of the screen (on the left side in the current example). Participants had to prepare their response as soon as the ball was presented but had to wait until the appearance of a bridge (imperative signal) to release their response. When the response was correct, the ball rolled on the bridge and reached the goal. A feedback reflecting how fast and accurate the subjects had been concluded each trial. (B) The response device. Index finger responses were recorded using a home-made device positioned under the left (graphic representation) and right (photographic representation) hands. (C) Time course of a trial. Each trial started with a blank screen (inter-trial interval) lasting for 2800ms. Then, the preparatory cue appeared for a variable delay period (550—700ms), followed by the imperative signal (duration determined on an individual basis based on the participant's RT, see below). The feedback was presented at the end of each trial for 500ms. In the TMS experiment, pulses either fell during the inter-trial interval (2300 ms after the blank screen onset; $TMS_{baseline\text{-}in}$), or during the delay period (500 ms after the preparatory cue onset; TMS_{delay}). Motor-evoked potentials (MEPs) were elicited in the first dorsal interosseous (FDI) of both hands using a double-coil TMS procedure. In SAS trials, the sound always occurred concurrently with the TMS pulse, either at $SAS_{baseline}$ (TMS experiment only) or SAS_{delay}. The figure displays a left hand trial with a SAS and a TMS pulse during the delay period. (D) Double-coil$_{1ms}$ TMS protocol. Two small figure-of-eight shaped coils were placed over the left and right primary motor cortex (M1), eliciting MEPs in the left and right FDIs on each trial, at a near simultaneous time (1ms delay).

Experimental procedure

Experiments were conducted in a quiet and dimly-lit room. Participants sat in front of a 21-inch monitor screen positioned about 60 cm in front of them. Their arms were semi-flexed with both hands resting palm-down on a response device developed in our laboratory to detect any horizontal movement of the index fingers (Fig. 1B). This setup has the advantage of delivering a very precise measure of the RT (precision = 1ms) and to control the initial index finger position at the beginning of the trial. Moreover, as the metal parts are mobile, they can be placed according to the morphology of each participant (for more details regarding this device, please refer to [53]).

Each trial was composed of several events (Fig. 1C). It first started with a blank screen lasting for 2800 ms. Then, the preparatory cue appeared, which consisted of the ball and the goal separated by a gap. Subjects were explicitly told to prepare their response based on the position of the ball but to withhold it until the onset of the imperative signal (i.e. the bridge) which appeared 550 to 700 ms later. We purposely varied the duration of the delay period to decrease the subjects' tendency to respond prematurely (i.e. before the imperative signal). For the same reason, each block involved a few trials in which the bridge did not appear (i.e. catch trials — 4 per block). In these trials, subjects were required not to respond and were penalized if they did so. Once the bridge was on the screen, subjects had to respond as fast as possible to allow the ball to roll on it and to quickly reach the goal. Each trial ended with a feedback displaying a score for 500 ms. Subjects knew that this score would depend on how fast and accurate they had been on the previous trial. That is, on correct trials, scores were inversely proportional to the RT (i.e., the faster the subjects, the higher the score); they were displayed in green and ranged from 1 to 100 [59]. The RT was defined as the time interval between the bridge appearance and the time at which the responding index finger left the outer metal edge of the response device. Incorrect responses were penalized, as indicated by negative scores displayed in red. They involved (1) responses occurring too early, referred to as anticipation errors (penalized by − 75 points), (2) responses occurring too late, referred to as time out errors (penalized by − 50 points), (3) responses provided with the incorrect hand, referred to as choice errors (penalized by − 80 points) and (4) responses provided on catch trials, referred to as catch errors (penalized by − 75 points). Anticipation errors consisted in responses provided either before the bridge onset or after its onset but with a RT smaller than 90 ms: below this time, we consider that the response was released prematurely (i.e. before detection of the bridge) given the fixed time required for visuo-motor conversion to occur [57]. Time out errors consisted in responses provided after the bridge offset (determined on an individual basis, see below). Note that when subjects succeeded not to respond on a catch trial, they were rewarded by + 12 points. The total score was displayed at the end of each block.

In some trials, a SAS occurred. This consisted of a narrow band noise pulse (1 kHz, 40 ms, 118 decibel) produced and presented via headphones (Harman International [Stamford, USA] Model AKG K430). The sound was calibrated by a Digital Sound Level Meter (SECOMP International [Bassersdorf, Switzerland] Model Roline RO1350) using the standard A-weighted decibel scale and measured 2 cm from the headphone speaker. Importantly, when applied during action preparation in RT tasks, a SAS can accelerate the initiation of the prepared movement [6,11,18,48,57]. As such, RTs are usually reduced on trials in which a SAS is presented at the imperative signal, and the extent of the shortening effect has led researchers to propose that such a loud sound prompts the release of preliminary motor plans that have already reached subcortical aspects of the motor output pathway [7,10,49], but see also [47] for opposing views.

Interestingly, the influence of SAS applied when subjects are actively withholding a movement following a fully informative preparatory cue, postponing its initiation until an imperative signal, is unknown. In fact, inhibitory influences are largely deployed during such delay periods [20] and these processes may reduce the impact of a SAS occurring at that time (SAS_{delay}), compared to when it is applied in regular RT tasks that do not explicitly require postponing a fully prepared response. Here, we aimed at testing the influence of a SAS_{delay} by applying it always 500 ms after the preparatory cue onset (i.e. falling −150 to −50 ms before the imperative signal) in the Rolling Ball task. Moreover, we were interested in investigating whether the impact of a SAS_{delay} can be reduced when it is anticipated, possibly through the strengthening of inhibitory influences serving to withhold prepared responses. To address this point, the probability of a SAS_{delay} was varied in two different types of blocks. In a first block type, SAS_{delay} were rare (R) occurring only in very few trials (6.6% and 3.3% trials for the behavioural and TMS experiment, respectively — RSAS blocks) whereas in the other block type, SAS_{delay} were more frequent (F), occurring in 26.6% and 18.8% of trials for the behavioural and TMS experiment, respectively (FSAS blocks). Subjects were always told about the type of block they would start performing next. Consequently, the degree to which subjects anticipated a SAS_{delay} clearly varied in these two contexts; it was smaller in the RSAS blocks than in the FSAS blocks. The order of the blocks was pseudo-randomized such that some subjects performed the RSAS blocks first and others the FSAS blocks first. Within each block, the order of trials was also pseudo-randomized in order to avoid having two trials with a SAS in a row [6,18]. In the RSAS context, an additional undisclosed rule was introduced: the SAS trials were separated by at least 7 trials without any sound. Each block consisted in an equal proportion of left and right hand trials. They lasted approximately 5 min and were run successively. Short breaks were made between the blocks.

Behavioural experiment

The behavioural experiment (n = 16) served to characterize the influence of a SAS_{delay} in the RSAS and FSAS blocks on the subjects' behaviour (RTs, anticipation and time out errors): we hypothesized that the occurrence of frequent SAS would generally increase cautiousness and prolong RTs in the FSAS blocks. Each experimental session involved 2 preliminary blocks of 60 trials followed by 8 testing blocks. The first block served to familiarize the subjects with the task. It consisted of 20 trials without any SAS, followed by 40 trials in which some SAS_{delay} were elicited (15% of the trials) to familiarize the subjects with the sound. Then, the second block was run to compute the individual's median RT. This block involved 60 trials in the absence of SAS. We used this RT measure to adapt the duration of the bridge presentation in the subsequent 8 testing blocks on an individual basis. As such, the duration of the bridge was set to correspond to the subject's median RT + 2 standard deviations (SD). Subjects were required to elicit a response within this time window. If subjects responded later, they were provided with a negative feedback. Based on pilot experiments, this procedure seemed optimal to force the subjects to prepare their movement in advance. After that, the actual experiment began with the 8 testing blocks. There were 4 RSAS blocks and 4 FSAS blocks, each involving 60 and 64 trials, respectively (same amount of left and right hand trials). The RSAS blocks consisted of 56 trials without SAS (including 4 catch trials) and 4 SAS_{delay} trials (6.6%); the FSAS blocks were composed of 44 trials without SAS (including 4 catch trials) and 16 SAS_{delay} trials (26.6%). For the behavioural data analysis, trials were separated according to whether responses were provided with the left or right hand, in the presence of a SAS_{delay} or not, in RSAS or FSAS blocks.

TMS experiment

The TMS experiment ($n = 11$) served to compare preparatory inhibition during the delay period in the RSAS and FSAS blocks. Similar to the behavioural experiment, each session started with 2 preliminary blocks that served to familiarize the participants with the task and to set the bridge duration. Then, the main phase of the experiment began, with 4 testing blocks, half of which were performed in a RSAS context (60 trials/block) and the other half in a FSAS context (64 trials/block). A TMS pulse was applied in each trial at one of two possible timings (Fig. 1C). To obtain a baseline measure of CS excitability, some trials involved a TMS pulse falling 2300 ms after the blank screen onset (22 trials per block [RSAS blocks] or 20 trials per block [FSAS blocks]), eliciting MEPs in the context of the task but during the inter-trial interval ($TMS_{baseline\text{-}in}$). In the remaining trials (38 trials [RSAS blocks] or 44 trials [FSAS block]), the TMS pulse was delivered 500 ms after the preparatory cue onset (TMS_{delay}) (Fig. 1C). MEPs elicited at TMS_{delay} were always sorted according to whether they fell in a hand that was selected for the forthcoming response ($TMS_{delay\text{-}selected}$) or non-selected ($TMS_{delay\text{-}nonselected}$). Based on previous studies, we assumed that, at this time, MEPs would be strongly suppressed, reflecting preparatory inhibition when subjects are withholding a motor response [20,39,53,60,66]. In addition to these probes of CS excitability within the blocks, MEPs were also elicited between the blocks to obtain a baseline measure of CS excitability outside the context of the task ($TMS_{baseline\text{-}out}$, 20 pulses between each block, each separated by a delay ranging from 3200 to 4000 ms).

Critically, in trials involving a sound, the SAS always occurred concurrently with the TMS pulse (Fig. 1C). That is, the SAS_{delay} always occurred at the same time as the TMS_{delay} pulse (500 ms after the preparatory cue onset, as in the behavioural experiment). Moreover, the TMS experiment also involved trials in which a SAS occurred during the inter-trial interval, at the time of $TMS_{baseline\text{-}in}$. We did not expect such $SAS_{baseline}$ to elicit a startle response as it has been shown that such a response only occurs when a movement is already planned [7,11]. However, we included some $SAS_{baseline}$ to make sure that a potential difference between MEPs elicited during the delay period or at baseline could not be explained by a different level of SAS expectancy at these two times. The RSAS blocks consisted of 56 trials without SAS (including 4 catch trials), 2 SAS_{delay} trials (3.3%) and 2 trials with $SAS_{baseline\text{-}in}$; the FSAS blocks were composed of 48 trials without SAS (including 4 catch trials), 12 SAS_{delay} trials (18.8%) and 4 trials with $SAS_{baseline\text{-}in}$.

Importantly, TMS was always delivered using a double-$coil_{1ms}$ TMS method recently developed in our laboratory [28—30,59,67]. Briefly, this method consists in a near-simultaneous stimulation of the two M1 (1ms inter-pulse interval), allowing to obtain MEPs in both hands at once (Fig. 1D). The short inter-pulse interval allows to avoid direct electromagnetic interference between the two coils, while preventing transcallosal interactions to occur between motor areas [26,37]; the MEPs obtained using this approach are comparable to those elicited using single-coil TMS, regardless of the pulse order [28,30,31,59,60]. In the present study, the first TMS pulse was always applied over the right M1, eliciting a first MEP in the left hand, followed shortly (1 ms later) by a MEP in the right hand.

The two TMS pulses were delivered through small figure-of-eight coils (wing internal diameter, 35 mm); the coil stimulating right M1 was connected to a Magstim 200 magnetic stimulator (Magstim, Whitland, Dyfed, UK) and the coil stimulating left M1 to a Magstim Super Rapid magnetic stimulator. The coils were placed tangentially on the scalp and the handle was oriented toward the back of the head and laterally at a 45 angle away from the midline, approximately perpendicular to the central sulcus. For each M1, the optimal scalp position for eliciting a contralateral MEP in the first dorsal interosseous (FDI) muscle was identified and marked on a cap placed on the subject's head to provide a reference mark throughout the experiment [19,58]. It was important to check that both coils could be positioned simultaneously on the head without touching each other. Minor adjustments were sometimes necessary without precluding the acquisition of optimum FDI MEPs [28,59,67]. The resting motor threshold (rMT) was determined as the minimal TMS intensity required to evoke MEPs of about 50 μV peak-to-peak in the relaxed FDI muscle in at least 5 out of 10 consecutive trials [16,17,19,68]. Across participants, the rMTs corresponded to $36.9 \pm 1.71\%$ and $53.8 \pm 2.98\%$ of the maximum stimulator output for the right and the left M1, respectively. The higher rMT value for the left M1 is due to the use of a Super Rapid Magstim on that side [23]. For each hand, the intensity of TMS throughout the experiment was always set at 115% of the individual rMT.

Electromyography recording

Electromyography (EMG) data were collected for 3200 ms on each trial, starting always 200 ms before the SAS/TMS pulse (or at the corresponding time in the absence of SAS in the behavioural experiment). Raw EMG signals were amplified (gain, 1 K), bandpass filtered online (10—500 Hz; NeuroLog; Digitimer) and digitized at 2000 Hz for offline analysis.

The presence of EMG activity in the sternocleidomastoid (SCM) in a time window from 30 ms to 90 ms after the occurrence of a SAS has been considered to be a sensitive indicator reflecting the occurrence of a startle response [10,11]. For this reason, we placed surface electrodes (Neuroline, Medicotest, Oelstykke, Denmark) on the left and right SCM and similar to previous investigations, we recorded the number of SAS trials in which the SCM EMG activity exceeded more than two standard deviations above the baseline level. This number was then expressed in percentage of the total number of SAS trials [11]. Surprisingly, only 31% of our participants displayed some SCM EMG activity following SAS. Moreover, in all these responsive subjects, SCM activity was only present in the first testing block but disappeared afterwards. Because such responses were rare, we did not further analyse them. Critically, previous studies have failed to observe dependable SCM activity following SAS [56]. Then, the fastening effect of SAS on RTs is still present but typically attenuated compared to when SCM activity is elicited. In this case, RTs are typically about 46 ms shorter than in control trials [43].

In the TMS experiment, additional electrodes were placed on the left and right FDI to measure MEP amplitudes.

For the MEP analysis, trials with any background EMG activity (root mean square computed in the 200 ms windows preceding the TMS artefact) exceeding 3 standard deviations (SD) around the mean were discarded for the following analyses. This was done to prevent contamination of the MEP measurements by significant fluctuations in background EMG [14,22,25]. The remaining MEPs were classified according to the experimental condition within which they were elicited. For each condition, trials in which the subjects made an error were discarded. Finally, we excluded trials with peak-to peak MEP amplitudes exceeding 3 SD around the mean. After having trimmed the MEP data, a minimum of 24.0 ($\pm$ 5.8) trials remained in each condition.

Statistical analysis

Behavioural experiment

Behaviour was assessed by considering RTs as well as the percentage of anticipation and time out errors for each subject; choice errors were rare and thus not analysed. RTs were analysed using a three-way repeated measure (RM) analysis of variance (Anova) with context (RSAS, FSAS), responding hand (left, right) and sound (No SAS, SAS_{delay}) as within-subject factors. For the analysis of anticipation and time out errors, we used separate two-way RM Anovas, with context and sound as within-subject factors (left and right hand trials were pooled together to increase the number of observations in each condition). Statistical significance was set at $P < 0.05$.

TMS experiment

For the analysis of CS excitability, we first considered MEPs (mV) at baseline. These data were analysed using a two-way RM Anova, including MEP-SIDE (left or right) and baseline-type ($TMS_{baseline\text{-}out}$, RSAS $TMS_{baseline\text{-}in}$, FSAS $TMS_{baseline\text{-}in}$) as within-subject factors. Then, to compare the strength of preparatory inhibition in the two block types, MEP amplitudes at $TMS_{baseline\text{-}in}$ and at TMS_{delay} were analysed with a three-way RM Anova, with context (RSAS or FSAS), MEP-SIDE (left or right) and TMS-condition ($TMS_{baseline\text{-}in}$, $TMS_{delay\text{-}selected}$, $TMS_{delay\text{-}nonselected}$) as within-subject factors. When appropriate, Anovas were followed by post-hoc tests, using the Fishers least significant difference (LSD) procedure. All data are expressed as mean $\pm$ standard error (SE). Statistical significance was set at $P < 0.05$.

Results

Behavioural experiment

Reaction times

Two participants were excluded from this analysis as they failed on too many trials in the RSAS context. More precisely, these subjects made a lot of anticipation and time out errors when a SAS occurred, precluding us from analysing their RT data. In the remaining subjects ($n = 14$), the average RTs were 200 ms (SE = 7.4) and 204 ms (SE = 7.2) in trials without SAS, in the RSAS and FSAS contexts, respectively. In the presence of a sound, RTs equaled 186.7 ms (SE = 10.4, $n = 14$) and 174 ms (SE = 7.6, $n = 14$) in the corresponding contexts. The three-way RM Anova performed on these data revealed a significant main effect of the factor sound ($F = 11.73$, $P < 0.01$): RTs were significantly reduced in trials including a SAS (Fig. 2A), consistent with previous studies showing that a loud sound can shorten RTs if triggered when a movement is being prepared in simple and choice RT tasks [8,27,41,46,57]. Our analyses also revealed a significant context X sound interaction ($F = 5.25$, $P < 0.05$). As such, although the presence of a SAS reduced RTs in both contexts (all $P < 0.05$), this shortening effect was more pronounced in the FSAS than in the RSAS blocks. Hence, the SAS led to faster responses when the sound had been anticipated ($P < 0.001$) compared to when it was unlikely ($P < 0.05$). In the absence of SAS, RTs were comparable in the RSAS and FSAS contexts ($P = 0.41$). Hence, contrary to our prediction, a high probability of SAS did not increase RTs (i.e. cautiousness) in FSAS blocks. Finally, we did not observe any effect of the responding hand on RTs (all $F < 2.10$ and $P > 0.17$).

Percentage of errors

Anticipation errors. The two-way RM Anova revealed a significant main effect of sound ($F = 25.79$, $P < 0.001$). By contrast, we did not observe a significant effect of context ($F = 0.78$, $P = 0.39$) or a sound X context interaction ($F = 1.80$, $P = 0.20$). As evident on Fig. 2B, subjects made more anticipation errors when a SAS_{delay} occurred compared to when it was absent, regardless of the context.

Time out errors. The two-way RM Anova revealed a significant context X sound interaction ($F = 7.28$, $P < 0.05$), in the absence of any main effect. As evident on Fig. 2C, the presence of a SAS_{delay} increased the percentage of timeout errors in the RSAS context ($P < 0.01$) but not in the FSAS context ($P = 0.96$), possibly because the sound was more disturbing when it was less expected.

TMS experiment

The TMS experiment was carried out on 11 participants but only 10 were included in the analyses because MEPs were abnormally high in one subject, exceeding 3 SD above the mean of the other participants, due to an error while establishing the rMT. When this subject was excluded, the mean MEP amplitude at $TMS_{baseline\text{-}out}$ was 1.65 mV (SE = 0.29, $n = 10$). Then, when elicited within the blocks, MEPs at $TMS_{baseline\text{-}in}$, equalled 2.60 mV (SE = 0.41, $n = 10$), and 2.27 mV (SE = 0.38, $n = 10$) in the RSAS and FSAS contexts, respectively. The two-way RM Anova performed on those data revealed a main effect of baseline ($F = 7.40$, $P < 0.01$). As evident in Fig. 3, MEPs were smaller when elicited at $TMS_{baseline\text{-}out}$ compared to TMSbaseline-in in the FSAS ($P < 0.05$) and RSAS ($P < 0.001$) contexts, respectively. Importantly, MEP amplitudes at $TMS_{baseline\text{-}in}$ were comparable in the two contexts ($P = 0.13$). Finally, we did not observe any significant main effect of MEP-SIDE ($F = 0.57$, $P = 0.47$) or a significant interaction between the two factors ($F = 0.33$, $P = 0.72$).

In order to assess the strength of preparatory inhibition in both contexts, a three-way RM Anova was performed on left and right FDI MEPs obtained at $TMS_{baseline\text{-}in}$ and TMS_{delay} preceding left and right hand responses (Fig. 4). Our analysis revealed a significant main effect of the factor TMS-condition ($F = 23.78$, $P < 0.001$), due to systematically

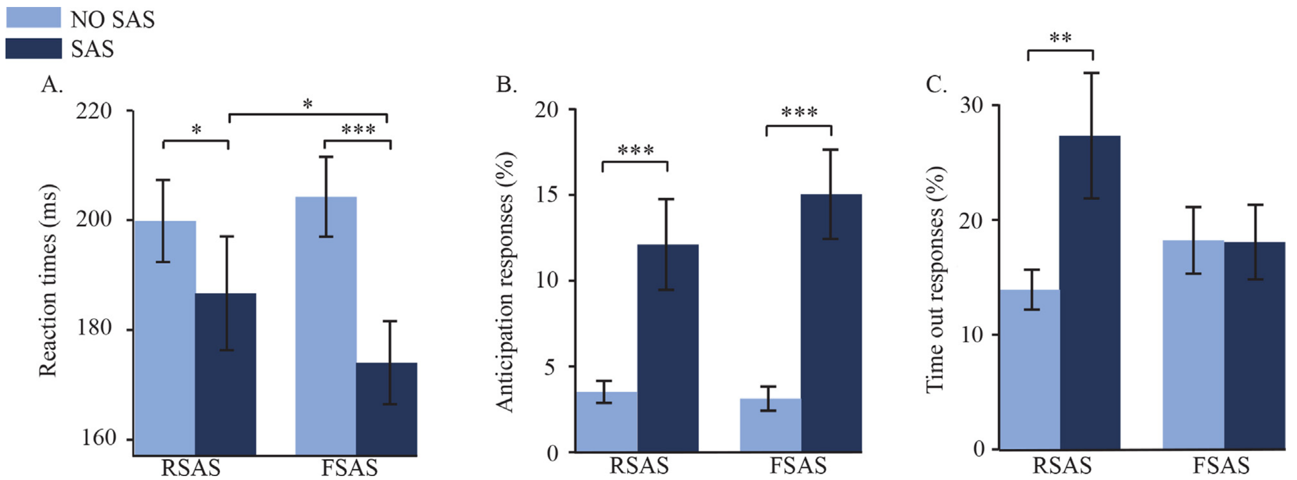

Figure 2 (A) Reactions times (RTs). Reaction times (ms) measured in both contexts (that is, rare (R) startling acoustic stimulus (SAS) resulting in RSAS context and frequent (F) SAS resulting in FSAS context) in trials with (light blue bars) or without (dark blue bars) SAS. Note that RTs were systematically shortened when a sound was elicited. In addition, RTs were significantly shorter in the FSAS context relative to the RSAS one in trials including a SAS. (B) Percentage of anticipation responses. Percentage of anticipation responses in both contexts in the presence or absence of a SAS. The presence of a SAS increased the percentage of anticipation responses, which confirmed its ability to induce a startle response. (C) Percentage of time out responses. Time out responses shown for trials in both contexts with or without a sound. Note the context X sound interaction, due to a significant increase in the percentage of time out responses when a sound was produced in the FSAS context only. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$. Error bars represent (SE).

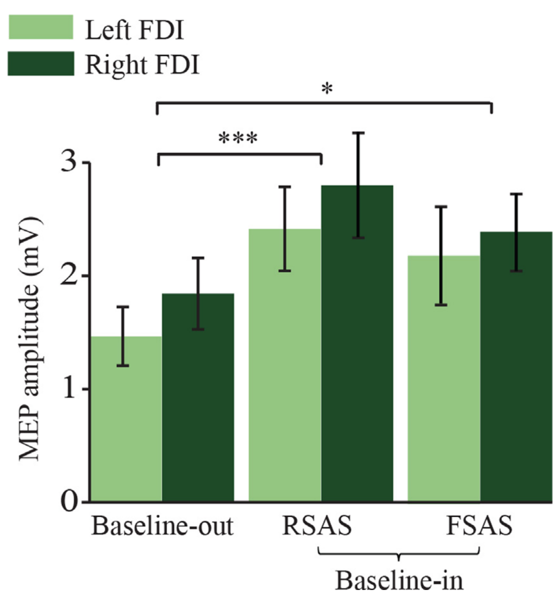

Figure 3 Change in motor-evoked potentials (MEPs) from baseline-out to baseline-in. Amplitude of first dorsal interosseous (FDI) MEPs (in mV) recorded in both hands between ($TMS_{baseline-out}$) or during ($TMS_{baseline-in}$) the blocks in the rare (R) startling acoustic stimulus (SAS) resulting in RSAS context and frequent (F) SAS resulting in FSAS context. MEPs were smaller at $TMS_{baseline-out}$ compared to $TMS_{baseline-in}$ in both contexts. $^{*}P < 0.05$, $^{***}P < 0.001$. Error bars represent (SE).

smaller MEPs at TMS_{delay} compared to $TMS_{baseline-in}$ (all $P < 0.001$). No other main effect or interaction between the different factors was found (all $F < 2.16$, $P > 0.14$). These results indicate that varying the probability of a SAS in the two contexts (RSAS or FSAS) did not significantly impact the strength of preparatory inhibition in the present study.

Discussion

Behaving in a goal-directed manner to fulfill short, middle and long-term goals requires the ability to refrain from automatic, stimulus-driven tendencies [44]. It is often assumed that the motor system plays a central role in this function, with its activity being shaped by overlapping control processes to favour goal-directed behaviours over premature or inappropriate responses [12,40,55]. Several control processes seem to involve inhibition of the motor system. Yet, the exact role of motor inhibitory changes is still largely debated [13,20,38,52]. One predominant hypothesis is that motor inhibition assists impulse control.

In the present experiments, we combined the TMS and SAS methodology in an instructed-delay choice RT task to deepen our understanding of the functional role of motor inhibition during action preparation. Importantly, we varied the rate of SAS in separate blocks, assuming that subjects would engage more impulse control to withhold their response during the delay period when SAS are expected (FSAS context) compared to when they are rare (RSAS context). More critically, we expected that enhanced impulse control in FSAS blocks would be associated with deeper preparatory inhibition. Results turned out to be very different from these predictions.

First, in the TMS experiment, MEPs showed a profound suppression during the delay period, consistent with previous studies [33,34,53,54,59]. However, this effect was comparable in both contexts. Hence, varying the probability of SAS did not influence the extent of preparatory inhibition implemented at the time of its potential occurrence.

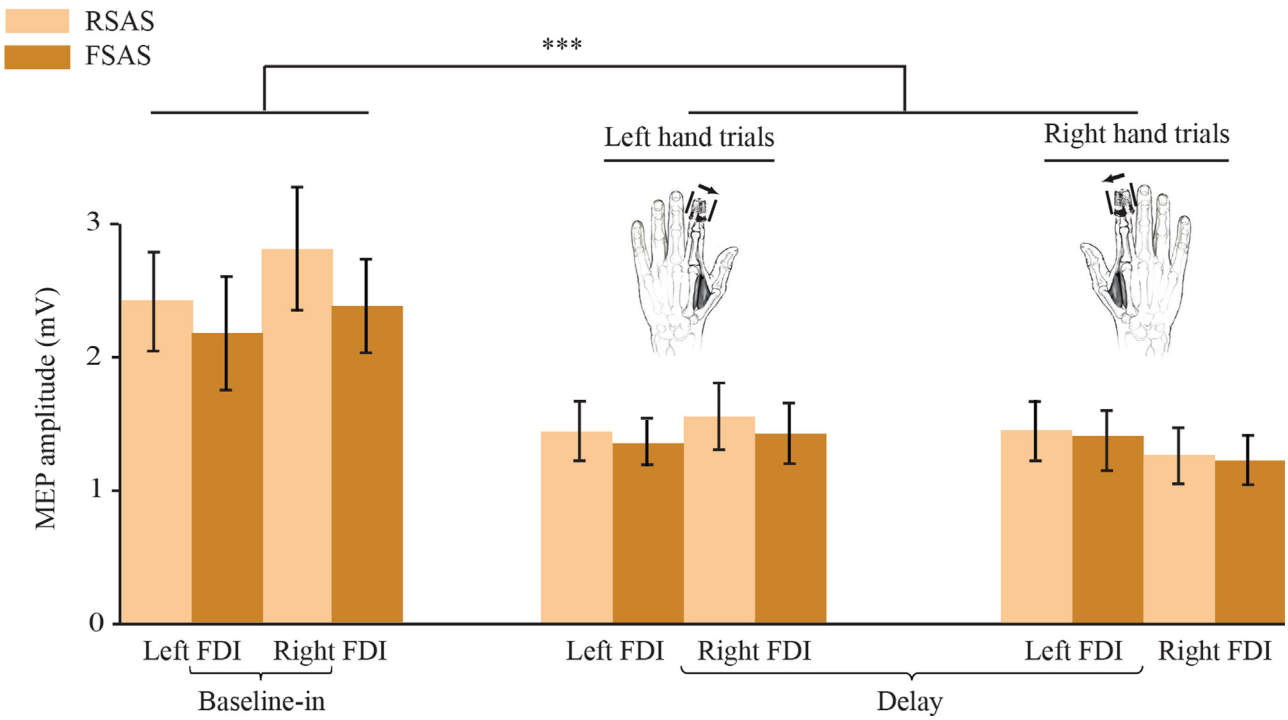

Figure 4 Change in motor-evoked potentials (MEPs) from baseline-in to delay. Amplitudes of MEPs recorded at $TMS_{baseline\text{-}in}$ and at TMS_{delay} in a selected or non-selected hand in the left and right first dorsal interossei (FDIs) in both block types (rare (R) startling acoustic stimulus (SAS) resulting in RSAS context — light orange bars — and frequent (F) SAS resulting in FSAS context—dark orange bars). Note the consistent suppression of MEPs at TMS_{delay} compared to $TMS_{baseline\text{-}in}$, reflecting comparable preparatory inhibition in the two contexts. $^{***}P < 0.001$. Error bars represent (SE).

Second, in the behavioural experiment, SAS elicited during the delay period reduced RTs, similar to when applied at the imperative signal in previous studies [8,57]. Yet, contrary to our predictions, this shortening effect on RTs was stronger in FSAS blocks than in the RSAS blocks, suggesting that increasing the frequency of SAS did not push subjects to recruit further impulse control. Consistently, in the absence of SAS, RTs were comparable in both block types, as were the anticipation errors. Interestingly, time out errors occurring following the presentation of a SAS were less common in FSAS than in RSAS blocks. Altogether, these results indicate that rather than augmenting impulse control resources, increasing the frequency of SAS might have increased the attention payed to the acoustic stimulus. Another non-exclusive possibility is that, on top of their startling effect, SAS induced some reactive inhibition, depending on the frequency (surprising effect) of SAS.

Impact of SAS expectation on subjects' behaviour and preparatory inhibition

Several previous studies have shown that manipulating the probability of events or trial types in a given block can vary the strength of control processes engaged in the task. For instance, it has been shown that increasing the proportion of incongruent trials in the Flanker task increases the amount of impulse control resources engaged in the task [15,25,40]. Contrary to our predictions, increasing the probability of SAS in the present study did not produce such an effect, although subjects were explicitly required to withhold their response even in the presence of SAS. As such, we did not observe any evidence for increased impulse control in FSAS compared to RSAS blocks: subjects did not slow down in the former context and the boosting effect of the sound was not attenuated. Such a negative effect in the present study may be due to the fact that subjects did not need to rely on such control process to succeed in the task, even in FSAS blocks. As such, the presence of preparatory inhibition during the delay period might be sufficient to handle the occurrence of SAS at that time and avoid premature responding, while complying with the instruction to respond fast.

One interesting finding here is that increasing the probability of SAS enhanced their shortening effect on RTs and reduced the amount of trials in which they produced time out errors. This finding may be due to the fact that subjects payed more attention to the sound in the FSAS than in the RSAS context, consistent with a recent study [45]. In that study, the authors performed two experiments showing that the level of attention participants pay to a specific sensorial modality (either a tone or a figure) can strongly affect the release of motor responses when SAS are presented. Hence, in the present experiment, it is possible that participants shifted more their focus on the sound in the FSAS than in the RSAS context.

Another, non-exclusive, possibility is that, on top of their startling effect, SAS induced some inhibition of motor activity and that this effect depended on the frequency (surprising effect) of SAS. This idea is consistent with a recent line of research showing that surprising events can produce inhibition of the motor system in a way that resembles reactive inhibition following stop signals [20,62,63]. In fact, it is likely that increasing the probability of SAS reduced their surprising effect and thus the strength of the associated reactive inhibition that might have occurred on top of preparatory inhibition. Unfortunately, here we focused on preparatory inhibition occurring at the time of the SAS but did not apply TMS at later time points to measure reactive inhibition after the SAS occurrence, which would have allowed us to address this point directly. Yet, we propose that reactive inhibition is likely to have been stronger in the RSAS context, reducing the boosting effect of the SAS on RTs and increasing time out errors, an interesting hypothesis for future investigations.

Limitations in the present studies

Some limitations in the design of the present study should be considered before drawing conclusion about the effect of SAS expectancy on preparation inhibition. First, we think it would have been useful to include a block type with no SAS at all in the present study. As such, although the SAS were rare in the RSAS blocks, their presence might have already changed preparatory inhibition, with no further modulation in FSAS blocks. Second, due to technical constraints, we were forced to present SAS through headphones and their use is known to be less efficient in producing startle responses compared to loud speakers. As such, in a recent study using headphones, Maslovat, Franks, et al. (2015) only observed SCM activity in 28% of trials, in contrast to the 80% (or more) usually observed when using a loud-speaker [7,8]. Here too, SAS only rarely induced SCM activity. Finally, the literature shows that at least 10—15% of people are non-responsive to SAS. That is, a SAS never (or only very rarely) induces a startle response in this population [1,9]. Here, we did not have enough subjects to cluster them into two categories (SAS responders vs SAS non-responders), yet this would be interesting in future studies.

Conclusion

These experiments support and extend previous work, which has revealed that preparatory inhibition is at play during motor preparation [4,24,33,34,59]. They are also in keeping with the studies of Carlsen et al. (2004) and Valls-Solé et al. (1999) who showed a significant decrease of RTs when a SAS is elicited.

Additional studies are required to investigate whether the lack of difference of preparatory inhibition between the two contexts is due to limitations in the task design and whether variations in preparatory inhibition can be evidenced with the use of loudspeakers, the inclusion of blocks without any SAS and the segregation of subjects according to their SAS sensitivity. These studies should also include TMS pulses after the SAS to measure the potential occurrence of reactive inhibition due to their surprising effect.

Disclosure of interest

The authors declare that they have no competing interest.

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