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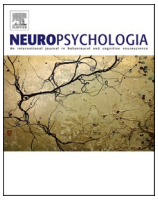

TMS reveals distinct patterns of proactive and reactive inhibition in motor system activity

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ABSTRACT

Response inhibition is our ability to suppress or cancel actions when required. Deficits in response inhibition are linked with a range of psychopathological disorders including addiction and OCD. Studies on response inhibition have largely focused on reactive inhibition—stopping an action when explicitly cued. Less work has examined proactive inhibition—preparation to stop ahead of time. In the current experiment, we studied both reactive and proactive inhibition by adopting a two-step continuous performance task (e.g., "AX"-CPT) often used to study cognitive control. By combining a dot pattern expectancy (DPX) version of this task with transcranial magnetic stimulation (TMS), we mapped changes in reactive and proactive inhibition within the motor system. Measured using motor-evoked potentials, we found modulation of corticospinal excitability at critical timepoints during the DPX when participants were preparing in advance to inhibit a response (at step 1: during the cue) and while inhibiting a response (at step 2: during the probe). Notably, motor system activity during early timepoints was predicted by a behavioural index of proactive capacity and could predict whether participants would later successfully inhibit their response. Our findings demonstrate that combining TMS with a two-step CPT such as the DPX can be useful for studying reactive and proactive inhibition, and reveal that successful inhibition is determined earlier than previously thought.

Inhibitory control is the ability to suppress situationally inappropriate thoughts and actions to meet personal goals and environmental demands. Our capacity for inhibitory control—especially when it is engaged rapidly and flexibly—determines our success in adapting to unexpected situations and is predictive of outcomes throughout life, such as academic performance and health (e.g., Diamond, 2013). Many psychopathologies are characterised by inhibitory control deficits, such as the failure to inhibit inappropriate thoughts or repetitive actions in OCD (e.g., Chamberlain et al., 2005); the failure to refrain from reward-seeking behaviour in addiction disorders; or the failure to suppress distracting thoughts or motor impulses in ADHD (e.g., Barkley, 1997).

Although there are many facets of inhibitory control (e.g., inhibition of thoughts, emotions, and motivations; e.g., Logan and Cowan, 1984), research has often focused on the inhibition of motor actions—that is, response inhibition—for both pragmatic and theoretical reasons. One key advantage of response inhibition compared with other forms of inhibition is that response inhibition can be easily measured and operationalised in behaviour through the withholding of a prepotent action. Response inhibition is also a ubiquitous function in daily life, and is impaired across a range of impulse control disorders. Moreover, it is thought that response inhibition likely engages neural and cognitive mechanisms that overlap with other forms of inhibition (Aron, 2011). Thus, advancing our understanding of response inhibition also advances our understanding of inhibitory control more generally.

Neurophysiological investigations of the motor system have played an important role in improving our knowledge and models of response inhibition. Studies using fMRI, EEG, and TMS have revealed much about the cognitive processes and neural mechanisms underlying the stopping network, including the inferior frontal gyrus, presupplementary motor area, subthalamic nucleus, striatum, and primary motor area (e.g., Aron et al., 2014; Chambers et al., 2009; Swann et al., 2012). However, the majority of this work has focused on reactive inhibition, that is, cancelling a response when signalled by an external cue—such as slowing when you catch sight of the brake lights in a car ahead. Sophisticated methods have been devised using go/no-go and stop signal tasks in combination with TMS to study the trial-by-trial dynamics of corticospinal excitability and reveal the reactive changes in motor

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preparation and inhibition (e.g., Chowdhury et al., 2019; Seet et al., 2019). In contrast, less is known about the cognitive and neural mechanisms underlying proactive inhibition—that is, preparing ahead of time to cancel a response in accordance with internally-maintained goals and expectancies—such as slowing before you approach a busy intersection expecting that there will be traffic ahead.

In many real-world situations, proactive inhibition is arguably more useful for controlling impulses, and researchers have emphasised a need to consider reactive and proactive inhibition separately (Aron, 2011). Proactive inhibition has been examined using a number of different behavioural paradigms (e.g., Chikazoe, et al., 2009; Verbruggen and Logan, 2009), but nonetheless remains a challenging construct to operationalise compared to its reactive counterpart. For example, researchers have used block-based manipulations of proactive inhibition comparing performance on inhibition blocks (including *no-go* or *stop* trials) with no inhibition blocks (including only *go* trials), or rely on task-level measures of proactive inhibition such as deliberate response slowing (i.e., *strategic slowing*; see Elchlepp et al., 2016). While useful, these measures are limited in their ability to capture the dynamic and flexible nature of proactive control because they rely on macro (block- or task-level) changes in performance across many trials. In doing so, they also rely on changes that could be attributable to any number of mechanisms involved in goal maintenance, motivation, or reinforcement. Other strategies for studying proactive inhibition include variations on the stop signal task (e.g., Jahfari et al., 2010) where participants are instructed in advance to conditionally stop only one response (e.g., right response) in the presence of the stop signal, but to ignore the stop signal for alternate response (e.g., left response; see also Cai et al., 2012; Greenhouse et al., 2012 for related work). Nevertheless, there is a need for more complex tasks that capture the breadth of processes required for proactive inhibition.

Here, we took inspiration from the cognitive control literature by adopting a two-step continuous performance task (CPT; Cohen et al., 1999; Servan-Schreiber et al., 1996) to develop a TMS protocol that investigates reactive and proactive inhibition influences on corticospinal excitability. The challenges of separating proactive and reactive processes in response inhibition mirror similar theoretical considerations in the study of cognitive control, defined as the ability to hold in mind contextual, task-related information to flexibly adapt behaviour in accordance with internally maintained goals. In the context of two-step CPTs, such as the AX-CPT and other similar tasks, proactive control is typified as planning that involves the maintenance of task goals in working memory, while reactive control involves the selective retrieval of goal information on an as-needed basis (Braver, 2012). Thus, these constructs of proactive and reactive control have a strong correspondence with the constructs of proactive and reactive inhibition in their requirement for goal maintenance (the possible need to stop soon) and goal retrieval (the imperative to stop now).

The two-step "AX" variant of the CPT has proven very useful for measuring both proactive and reactive control (Braver, 2012; Cohen et al., 1999; Servan-Schreiber et al., 1996). In the AX-CPT, a participant is presented with a cue stimulus (A or B in step 1), followed by a delay, and then a probe stimulus (X or Y in step 2). Participants are required to make a 'target' response only following an 'AX' pair, but to make a non-target response for all other pairs: AY, a target cue followed by any non-target probe; BX, a non-target cue followed by a target probe; and BY, which consist of a non-target cue and non-target probe. Studies varying the proportion of AX-AY-BX-BY trials (e.g., Dias et al., 2003; Henderson et al., 2012) have found that the frequency of the target (AX) pairs has a great influence on the response demands, and in turn, the control demands in the task. In typical versions of the AX-CPT task (and the version used in the current experiment), because AX pairs comprise the majority of trials, they engender a preparatory context triggered by the A cue, and a strong bias for the target response triggered by the X probe. Having the default mode of the task as one that requires response preparation and implementing a two-step design with the insertion of a time window between the cue and the probe is critical for observing a reliable pattern of proactive (BX) and reactive (AY) errors.

Individuals employing effective proactive control will represent and maintain the goal information provided by cue A and cue B. As a consequence, these individuals make less commission errors on BX trials (i.e., less likely to make a target response on a nontarget trial), but this can come at the expense of making more commission errors on AY trials. In contrast, individuals with effective reactive control will respond primarily using goal information retrieved at the time of the probe—as a consequence, these individuals tend to show the reverse pattern, making more commission errors on BX trials, but fewer commission errors on AY trials. Thus, the two-step variant provides an assessment of goal representation during the cue, goal maintenance during the delay between the cue and probe, and goal updating during the probe. Previous studies have found that younger adults typically rely on a proactive, cue-based strategy while older adults rely more on a reactive, probe-based strategy (e.g., Braver et al., 2001; Braver et al., 2009; Paxton et al., 2008). Specifically, younger adults tend to make fewer BX errors as they maintain the goal following the B-cue more effectively, but make more AY errors as maintaining the goal following the A-cue can lead to a prepotent target response, due to the frequent pairing of cue A and probe X. In contrast, older adults tend to show the reverse pattern, making more BX errors and fewer AY errors, as they update the goal based on the information provided by the probe.

Cognitive control research using the AX-CPT has also been applied to clinical settings, most commonly in patients with schizophrenia (e.g., Barch et al., 2001; MacDonald and Carter, 2003). Past research found that patients with schizophrenia were selectively impaired on BX, but not AY trials compared with controls, suggesting that this pattern of errors stemmed from selective deficits in proactive maintenance of the cue-related (contextual) information, but not reactive decisions based on the probe information. Additionally, using fMRI in combination with the AX-CPT, these same studies and others (e.g., Lesh et al., 2013) showed that the BX errors were related with disturbances in dorsolateral prefrontal cortex activity, suggesting that proactive control deficits in clinical populations are closely link with brain regions implicated in goal maintenance.

Neuroimaging studies with the AX-CPT using fMRI are useful for revealing associated brain areas recruited across different control modes, but they lack the temporal resolution to track how activity changes during the highly dynamic task. Research using EEG has made some progress in this area, showing that the identity of the probe produces distinct patterns of EEG activity (e.g., Bekker et al., 2004; Dias et al., 2003). These studies used a version of the AX-CPT where the target response following AX trials ("go" trials) remained the same but the non-target response following all other trial types was replaced with no response ("no-go" trials). However, past research has focused on comparing activity between go versus no-go probes and the results from such studies (e.g., Bekker et al., 2004) do not reveal differences in proactive and reactive control processes during the probe. It is the comparisons between the various no-go trials (AY vs BX vs BY) that is most critical for separating proactive and reactive processes in the task. Neuroimaging studies that separate probes by AX, AY, BX, and BY trial types are difficult to conduct because large trial numbers are required for sufficient samples of each trial type (see Dias et al., 2003 for alternative approach, relying on 'global' task differences to make inferences about control modes).

Given the challenges associated with measuring state changes in brain activity between different control modes, past studies have not yet mapped the local, moment-by-moment variations within the AX-CPT during both proactive and reactive control processes. To precisely track motor preparation and inhibition, we use TMS to measure corticospinal excitability at critical timepoints throughout a trial during the cue and probe periods. When TMS is applied over the motor cortex, muscle activity is elicited in the contralateral hand that can be measured as a motor-evoked potential (MEP). MEPs provide a near-instantaneous

read-out of motor system activity at the time of stimulation and are sensitive to motor preparation and inhibition changes in cued response tasks (e.g., Bestmann and Duque, 2016; Poole et al., 2018; Tran et al., 2020). By using TMS while participants perform the AX-CPT, our study design leverages the proactive (versus reactive) control processes supporting performance in the task, and examines how motor preparation and inhibition affects excitability in the motor system at key timepoints around the cue and the probe.

In the current experiment, MEPs were used to index momentary changes in corticospinal excitability as a neural correlate of proactive and reactive inhibition during a structurally identical version of the AX-CPT, termed the dot pattern expectancy (DPX) task. This version of the task uses Braille-like dot patterns instead of letters as cue and probe stimuli. The DPX task requires fewer trials to measure proactive versus reactive control, and its stimuli do not rely on phonological processing (Barch et al., 2009; Henderson et al., 2012; Otto et al., 2014; Lopez-Garcia et al., 2016). Following a number of past AX-CPT studies, we adopted a go/no-go version of the DPX task (e.g., Dias et al., 2003; Bekker et al., 2004; Bickel et al., 2012; Dias et al., 2011), for which participants are instructed to only respond on target AX trials. This version of the task avoids any confounding activity attributable to non-target response processes associated with the contralateral hand.

Using a go/no-go DPX task, we inspected the temporal signatures of proactive and reactive inhibition, testing four key hypotheses. First, we investigated when proactive differences in motor system activity between A and B trials emerged; we expected that differences in corticospinal excitability would appear during A versus B cue presentations (hypothesis 1), despite no response being required at this time. Second, we investigated corticospinal excitability during the probe presentation; we expected that activity for AX trials would increase over time, while activity for AY, BX, and BY would remain relatively low (hypothesis 2). Such a pattern of corticospinal excitability reflects motor preparation in the case of the go trial (AX) and motor inhibition in the case of the no-go trials (AY, BX, and BY). Our next two hypotheses focused on the activity difference *between* the no-go trials. Third, we investigated whether MEPs on AY trials would initially rise then fall, reflecting the prepotency of the go response to the A cue, followed by reactive inhibition to the Y probe (hypothesis 3). Finally, we investigated whether MEPs on BX trials would be initially low but later rise, reflecting a conditioned motor preparation based on the frequent association with responding and the X probe (due to the majority of target AX trials; hypothesis 4).

In addition to our hypotheses about how motor system activity is modulated during the various DPX trial types, we examined whether the neurophysiological signatures of reactive and proactive inhibition were related to *individual differences* in proactive capacity, and if corticospinal excitability differed between *successful versus unsuccessful* inhibition. The ability to withhold responding on AY trials is thought to reflect reactive inhibition based on the Y-probe, and thus the state of the motor system at the probe onset may be particularly important for determining success or failure. However, on B-cue trials, which are thought to engage proactive inhibition, the critical test was whether activity at earlier time points, around the time that the cue is processed, would be different for successful and unsuccessful trials.

1. Methods

1.1. Design

The experiment was a within-participant design with 4 DPX trial types (AX, AY, BX, BY) and 6 TMS timepoints (at the fixation cross offset, at the cue offset, at the probe onset, 100 ms after the probe onset, 200 ms after the probe onset, and 300 ms after the probe onset).

1.2. Participants

Participants were first- and second-year undergraduate students from The University of Sydney enrolled in a Psychology course. The students participated as part of course credit and signed up voluntarily based on a short study description. Each participants completed a risk-questionnaire when they signed up for the study and again when they arrived in the lab. All procedures were approved by the human research ethics committee of The University of Sydney (2016/920).

Sample size calculation was estimated using effect sizes from previous TMS studies (e.g., Poole et al., 2018), and 30 participants was sufficient to detect a medium to large effect in a within-participant design with 80% power. Therefore, we aimed to have at least 30 participants in the final sample; collecting more than 30 participants is useful for having at least our target sample size after exclusions due to the TMS procedure. Based on the response rate to the online advertisement, 34 participants signed up to the experiment before we deactivated the study advertisement. All 34 participants completed the study; two participants completed 5 out of 6 blocks of the experiment and we included their data in the analysis. One participant was excluded because reliable MEPs could not be elicited in their right hand (more than half of the recorded MEPs were <50 μV). Another participant was excluded for having zero MEP samples in one of the cells and less than half the total number samples in three of the cells. The final analysis was conducted on 32 participants (Mean age = 19.75, SD = 2.13; Female = 22, Male = 9, Prefer not to specify = 1; Right-handed = 29).

2. Materials

2.1. Apparatus and stimuli

The experiment was conducted on a PC using PsychoPy (v2020.2.10). Stimuli were presented on a 24-inch monitor at a viewing distance of approximately 40 cm. The dot patterns (approximately 512 × 512 pixels) were arrangements of circles presented on a black background. White circles patterns were used for the cues and blue circle patterns were used for the probes. There were three different cue pattern configurations, and these arrangements could be filled or unfilled. There were two different probe pattern configurations. Two of the three cue configurations were randomly selected as the A and B cues; assignment of the cue configurations was counterbalanced across participants.

2.2. EMG and TMS

Three electrodes were attached to the right-hand for EMG recording. In preparation for recording, the skin was first exfoliated with a small sponge and then wiped with 70% v/v isopropyl alcohol at the site of the electrodes. Two 10-mm diameter Ag/AgCl electrodes were placed in a belly tendon arrangement over the first dorsal interosseus (FDI) muscle to measure MEPs. One ground electrode was placed over the ulnar styloid process of the wrist. EMG activity was recorded from 100 ms prestimulation to 400 ms post stimulation. This signal was digitally converted (sampling rate: 4 kHz, bandpass filter: 0.5 Hz to 2 kHz, mains filter: 50 Hz, and anti-aliasing) using LabChart software (Version 8, ADInstruments).

TMS was administered using a MagStim 200^2 stimulator and a 70 mm figure-eight coil. Participants wore an elastic cap marked with the 10/20 EEG electrode positions to help locate the hand region of the motor cortex. The coil was held tangentially to the scalp with the coil oriented 45° from the midline. The motor cortex "hotspot" was located by starting from a position 5 cm lateral and 1 cm anterior to the C_z. The coil was then moved around until the maximal MEP was elicited in the FDI. Once the hotspot was determined and marked, the participant was asked to place their head on a chin and forehead rest for the coil to be locked in position with an adjustable mechanical arm (Manfrotto). Resting motor threshold (rMT) was defined as the lowest stimulation intensity that produced a minimum of 50 μV in 5 out of 10 consecutive trials (Rossini et al., 2015). During the experiment, the stimulation intensity was set to 120% of rMT. The mean rMT of all participants who

started the experiment was M = 42.29, SD = 11.63 (n = 34). Participants were asked to keep their head still during thresholding and while the experiment was in-session, but they could move any other time.

Since we employed a within-participant design where all trials and conditions were experienced by each participant and because TMS was used to measure our dependent variable rather than used as a manipulation for our independent variable, there was no need for a sham TMS condition in our experiment. Any peripheral effects of the TMS (tactile and auditory) are matched across all conditions when measuring MEPs.

2.3. Procedure

The participants were provided with written instructions displayed on-screen that were supplemented with verbal instructions from the experimenter. The instructions included visual examples of the white cue and blue probe dot patterns subsequently used in the experiment. The participant was informed that the 'target' AX dot pattern pair depended on the configuration of the dot patterns; the filled or unfilled circles in the cue pattern did not matter. The participants were shown both combinations of the possible AX targets, one where the cue pattern contained filled circles and another where the cue pattern contained unfilled circles. The participants then completed a practice phase with 8 AX trials, 2 AY trials, 1 BX trials, and 1 BY trials presented in a pseudorandomised sequence. Once the practice phase was complete, the experimenter confirmed that the participant understood the task. Both the practice and the experimental phases included feedback using three auditory tones: a "chime" for correct go or no-go responses (hits and correct rejections), a "buzz" for incorrect go responses (false alarms), and a "knock" for time outs (misses).

The trial structure (see Fig. 1) of the practice and experimental phases were identical except TMS was triggered during the experiment. Trials started with an 800 ms blank screen followed by a 1000 ms fixation cross. The cue was then presented for 1000 ms followed by a 1000 ms cue-probe interval where a fixation cross remained on screen. A cue-probe interval of 1000 ms has been used in previous research (e.g., Braver et al., 2005; Barch et al., 1997), and it has been demonstrated that shorter delay intervals can reduce the task duration without compromising reliability and validity (Henderson et al., 2012). The probe was presented for 500 ms and the screen remained blank until the end of the trial. There was a 1200 ms response window from the onset of the probe where participants could make a response and this timing remained fixed regardless of whether a response was made. Auditory feedback was provided at the end of the response window. Participants were asked to respond as quickly and accurately as possible by pressing the space key with their right index finger for target AX (go) trials, but to withhold responding on all other (no-go) trials.

During the experiment, TMS pulses were delivered at one of six timepoints on every trial: at the offset of the first fixation cross, at the offset of the cue, at the onset of the probe (or offset of the second fixation cross), 100 ms after the onset of the probe, 200 ms after the onset of the probe, or 300 ms after the onset of the probe. The design required an adequate minimum number of TMS samples (24) at each timepoint for each condition. Once the probe is presented, there are 4 distinct trial types (AX, AY, BX, BY). However, prior to processing the probe (at cue offset and at probe onset), trials are classifiable in terms of the A or B cue that has been presented, which allows the design to collapse across probe designation (i.e., AX and AY trials prior to the probe can be groups as A trials, and BX and BY trials prior to the probe can be groups as B trials; see Table 1. Similarly, at fixation, samples can be collapsed across all trial types.

To ensure a minimum number of TMS samples and constrain the proportion of trials to have a majority of AX patterns, the experiment approximated a 70-10-10-10 (AX-AY-BX-BY) percentage of trials (AX70; e.g., Dias et al., 2011; Bickel et al., 2012). The experiment was split into

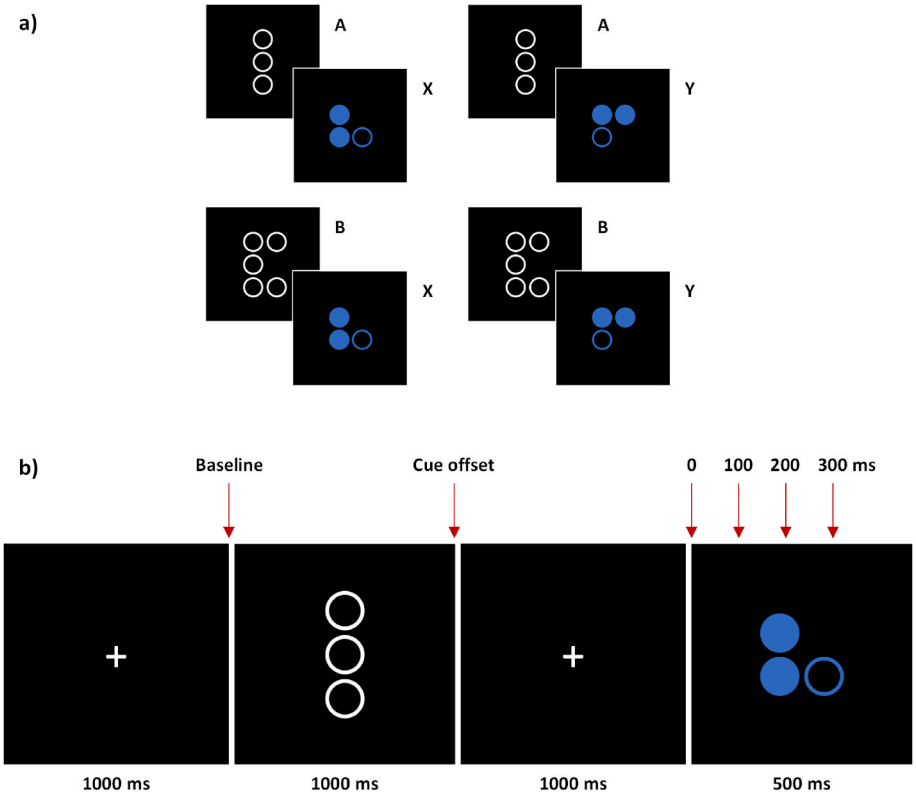

Fig. 1. Schematic of the DPX task. a) Example of AX, AY, BX, and BY trial type. White circles were used for the A or B cues, and blue circles were used for the X or Y probes. b) DPX trial structure with indicated TMS timepoints at Baseline (fixation offset), Cue offset, Probe 0 (Probe onset), Probe 100, Probe 200, and Probe 300. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Number of TMS samples by trial type and timepoint.

	Fixation	Cue	Probe 0	Probe 100	Probe 200	Probe 300
AX	33	84	84	168	168	168
AY	5	12	12	24	24	24
BX	5	12	12	24	24	24
BY	5	12	12	24	24	24

6 blocks. Each block contained at least 112 AX trials, 16 AY trials, 16 BX trials, and 16 BY trials (160 trials). An additional 8 "top-up" trials were split between the four trial types for a total of 168 trials per block. Each block was pseudorandomised in chunks of 42 trials, with each chunk containing a shuffled mix of 28 AX trials, 4 AY trials, 4 BX trials, 4 BY trials, and 2 top-up trials. The top-up trials were allocated to each of the four trial types such that after all 6 blocks, each participant received 1008 trials comprising 705 AX trials, 101 AY trials, 101 BX trials, and 101 BY trials. Each block lasted approximately 15 min and participants had a self-timed break between blocks where they were encouraged to move their head away from the chin and forehead rest, or to have a stretch before continuing. The experiment lasted approximately 90 min, and the entire testing session was approximately 120 min (5 min briefing, 20 min TMS setup, 90 min experiment, 5 min debrief).

2.4. Analysis

TMS samples were excluded if EMG activity in the window between 100 and 5 ms leading up to the TMS pulse had an amplitude greater than 50 μV or had a root mean square greater than 3 standard deviations. Additionally, TMS samples were excluded if participants made a response around the time when the TMS pulse was triggered as the MEP would be clearly contaminated with large activity. The MEP on these trials contain large artifacts in the EMG recording due to gross motor movements and represent actual motor execution rather than motor preparation (see Supplementary Material for the number of MEP samples retained separated by trial type and timepoint). Unless stated otherwise, mean MEPs are computed from trials where participants made a correct response on AX trials or successfully withheld their response on BY, BX, and BY trials. A separate analysis compared successful versus unsuccessful inhibition trials.

Data were analysed using JASP v0.16 and PSY Statistical Program where contrast confidence intervals are reported. The MEP data were split into three time periods to isolate the baseline period, proactive inhibition during the cue and pre-probe period, and reactive inhibition during the probe period. The baseline period included MEP data during the fixation timepoint. The pre-probe period focused on the effect of cue identity and included MEP data during the cue offset and probe onset (probe 0) timepoints. The probe period focused on the effect of the probe presentation and included MEP data during the probe 100, probe 200, and probe 300 timepoints. Note the division into three time periods can also be visualised in Table 1 by the collapsing of trials.

During the pre-probe period, the data were analysed as a 2 × 2 factorial design comparing A and B cues with the cue offset and probe onset timepoints. During the probe period, the data were analysed as a 4 × 3 factorial design comparing trial type (AX, AY, BX, BY) with the probe timepoints (probe 100, probe 200, probe 300). The four trial types were analysed as a set of orthogonal contrasts comparing AX trials against AY, BX, and BY trials (go trials vs no-go trials), AY trials against BX and BY trials (reactive inhibition vs proactive inhibition), and BX trials against BY trials (incongruent proactive trials vs congruent proactive trials). The three timepoints were analysed as an orthogonal set of linear, and quadratic trends. The two sets orthogonal contrasts do not require correction for multiple comparisons as they limit the per comparison error rate at $p = 0.05$. Since there were three probe timepoints, the highest order polynomial we could analyse was a quadratic trend. We expected the pattern of activity for AY trials would rise then fall (hypothesis 3), fitting a quadratic trend.

Additionally, we examined the relationship between MEPs and DPX performance. Due to considerable individual variability in overall MEP amplitudes, to compare the relative differences in motor system activity between two trial types, we standardised a difference score across participants by computing a log normalised ratio (e.g., Tran et al., 2021a). To compare performance on the DPX task, we used the proactive behavioural index (PBI, Equation (1)), a common measure of proactive control tendency (Braver et al., 2009; Gonthier et al., 2016; da Silva Castanheira et al., 2021). Since we used a go/no-go version of DPX task, we used error rates (cf. reaction times) to calculate PBI on the relevant trials.

Equation (1). Proactive Behavioural Index calculated on error rates of AY and BX trials.

$$PBI = \frac{AY - BX}{AY + BX} \quad (1)$$

Finally, we categorised the MEP data based on whether participants later successfully or unsuccessfully inhibited their response on the non-target no-go trials. To examine proactive inhibition, the data were analysed as a 2 × 2 × 2 factorial design comparing successful versus unsuccessful inhibition, AY versus B trials, and cue offset versus probe onset timepoints. Since the full 3 factor ANOVA model only included participants with values in all 8 cells, as a follow-up analysis we split the data by timepoint and compared the simple effects. Note, the simple effects have different degrees of freedom since participants had missing data in difference cells (e.g., some proactive participants only had unsuccessful inhibition on AY trials and none on B trials).

To examine reactive inhibition, the data were analysed as a 2 × 3 factorial design comparing successful versus unsuccessful inhibition with the probe 100, probe 200, versus probe 300 timepoints on AY trials. Similar to the proactive inhibition analysis above, the full 2 factor ANOVA model only included participants with values in all 6 cells, and simple effects were used as a follow-up analysis.

3. Results

3.1. Behavioural data

Participants generally performed well on the current version of the

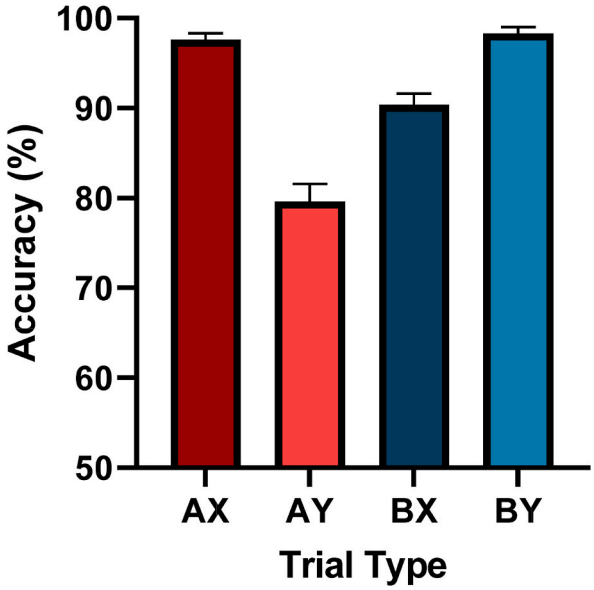

Fig. 2. Mean response accuracy by trial type. Error bars represent within participant standard errors.

DPX task (see Fig. 2). The lowest mean accuracy of the four conditions was 79.61% for AY trials. Performance on the task was assessed as a set of orthogonal contrasts comparing AX and BY trials against AY and BX trials (congruent trials vs conflicting trials where there is conflict established by the presence of the target cue or target probe), and AY trials against BX trials (reactive inhibition vs proactive inhibition). Accuracy was significantly higher for congruent cue-probe trials versus conflicting cue-probe trials, $F(1,31) = 114.67$, $p < 0.001$, 95% CI = 10.5%–15.4%, and accuracy was significantly lower for AY trials (where higher accuracy indexes reactive inhibition/control) versus BX trials (where higher accuracy index proactive inhibition/control), $F(1,31) = 17.45$, $p < 0.001$, 95% CI = 5.5%–16.0%.

The mean response time (RT) for AX trials was 406.65 ms, SD = 66.07, n = 32. For no-go trials in which participants made an incorrect response (commission errors), the mean RT for AY was 322.21 ms, SD = 52.43, n = 32; for BX was 520.78 ms, SD = 90.72, n = 30; and for BY was 389.29 ms, SD = 106.65, n = 22. The sample size of BX and BY trials is less than 32 because some participants did not make any response errors on these trials and hence we only report commission errors on no-go trials as descriptive statistics.

3.2. MEP data

Mean MEP as a function of DPX trial type and pulse time are depicted in Fig. 3 (see Figure S1, Supplementary Materials for normalised MEP). During the baseline period (fixation timepoint), we confirmed there was no significant effect of trial type, $F(3,93) = 1.19$, $p = 0.318$, $\eta_p^2 = 0.04$, and averaged over the conditions for a single point of reference. This analysis is important for establishing that the different trial types started from the same level of motor activity before the presentation of the cue or probe.

Pre-probe period (cue offset, and probe 0 timepoints): A vs B. MEPs were initially higher for A cues than B cues at the cue offset, but activity to the A cues then reduced to the level of B cues at the probe onset (probe 0). There was no significant effect of the probe for AX and AY, or BX and BY at these time points (Fs < 1; the probe identity has not yet been revealed to participants by these timepoints) so we averaged over AX and AY (cue A), and averaged over BX and BY (cue B). There was a marginal effect of timepoint such that MEPs were overall lower at the probe onset than the cue offset, $F(1,31) = 3.85$, $p = 0.059$, $\eta_p^2 = 0.11$. There was no significant effect of cue type, $F(1,31) = 2.01$, $p = 0.12$, $\eta_p^2 = 0.06$, but a significant cue type × time point interaction, $F(1,31) = 4.05$, $p = 0.009$, $\eta_p^2 = 0.12$.

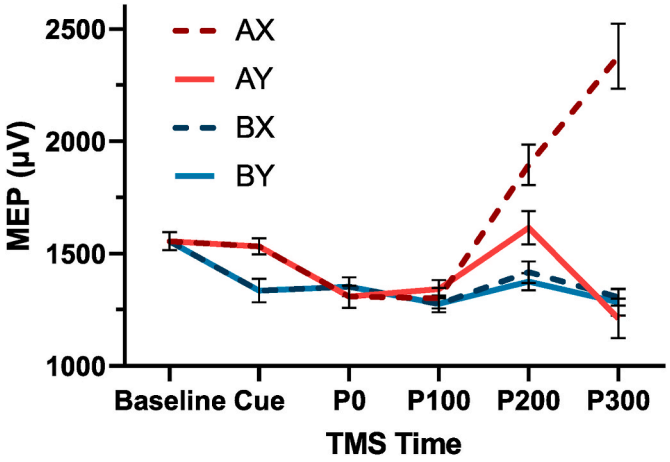

Fig. 3. Mean MEP by trial type and TMS time. Error bars represent within participant standard errors. Cue = cue offset; P = probe; MEP = motor-evoked potential; TMS = transcranial magnetic stimulation. Note that data are collapsed across trial type to a single data point at Baseline, and collapsed across probe type to form two data points (A-cue and B-cue trials) at Cue and P0 timepoints.

From inspection of Fig. 3, the interaction is due to participants having reduced MEPs for B cues compared to A cues during the cue offset, $t(31) = 3.92$, $p < 0.001$, $d = 0.69$, while this cue difference was absent at the probe onset, $t(31) = 0.64$, $p = 0.528$, $d = 0.11$. This interaction indicates that a difference in corticospinal excitability emerged during the cue period for A versus B cues, but was not sustained by the time of the probe onset.

Probe period (probe 100, probe 200, and probe 300 timepoints): AX vs AY, BX, BY. MEPs increased rapidly for AX trials, increased slightly before decreasing for AY trials, and remained relatively flat for BX and BY trials. There was a significant linear trend interaction between target go versus non-target no-go trials such that MEPs increased over the three timepoints for AX trials more than AY, BX, and BY trials, $t(31) = 11.88$, $p < 0.001$. The linear trend interaction reflects the escalation of motor system activity in the lead up to making a go response compared with the withholding of a response on the other trial types.

Probe period (probe 100, probe 200, and probe 300 timepoints): AY vs BX, BY. There was also a significant quadratic trend interaction between reactive inhibition and proactive inhibition trials such that MEPs increased then decreased for AY trials more than BX and BY trials, $t(31) = 2.64$, $p = 0.009$. From inspection of Fig. 3, the significant quadratic trend interaction is due to the presence of an inverted U (concave quadratic) function for AY trials that is absent on BX and BY trials. Isolating the quadratic interaction at each of the timepoints, participants had increased MEPs on AY trials at the Probe 200 timepoint compared to BX and BY trials, $t(31) = 2.61$, $p = 0.014$, $d = 0.46$, while this AY versus BX and BY difference was absent at the Probe 100 and Probe 300 timepoints, largest $t = 1.20$.

Probe period (probe 100, probe 200, and probe 300 timepoints): BX vs BY. MEPs on BX and BY trials exhibited a similar pattern across the three timepoints. Neither of the polynomic trends (linear or quadratic) significantly interacted with the two types of proactive inhibition trials (BX and BY), largest $t = 0.32$.

3.3. Individual differences in DPX performance

The MEP results exhibited a marked difference between A and B cues at the cue offset (Fig. 3). The magnitude of the MEP difference at this timepoint shows promise in acting as a neurophysiological marker of proactive inhibition. To assess this potential, we compared individual variability in the MEP difference between A and B cues with the PBI (Equation (1)). The PBI quantifies the relative interference on the critical AY and BX inhibition trials, where a larger PBI score indicates more utilization of cue-based contextual information (and less probe-driven behaviour). If corticospinal activity at the cue offset is related to behavioural expression of proactive inhibition, participants who show greater differentiation between activity to A versus B cues, should also score higher on the PBI. This relationship would suggest a correspondence between neurophysiological and behavioural indices of proactive inhibition.

We observed a significant correlation between the PBI and the log normalised MEP ratio of A and B cues at the cue offset. Participants with stronger behavioural expression of proactive control on AY versus BX trials (higher PBI) also exhibited larger relative MEP differences between A and B cues (higher log ratio indicating larger A cue MEP > B cue MEP difference), $r = 0.41$, $n = 32$, $p = 0.019$ (see Fig. 4). Critically, the PBI correlation was temporally specific—i.e., linked to the presentation of the cue, where we would expect proactive engagement—and did not correlate with the same neurophysiological measure at the probe onset, $r = -0.17$, $n = 32$, $p = 0.349$. Further, these two correlations were significantly different from each other, $z = 2.41$, $p = 0.008$.

Although using PBI as a measure of proactive planning is consistent with the literature, we note that PBI can vary as a function of AY error rates (reactive inhibition) even when BX errors rates (proactive inhibition) are held constant. Therefore, we additionally ran the same correlations with BX accuracy in place of PBI and found the same pattern of

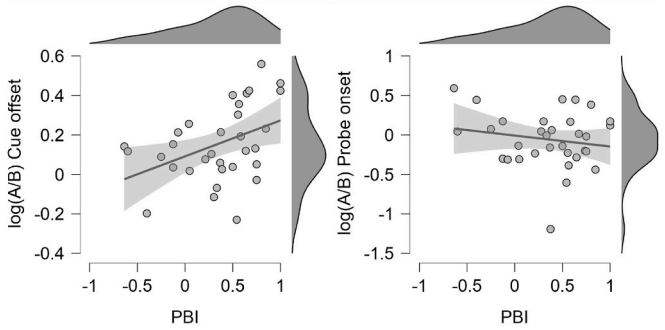

Fig. 4. Correlation between PBI and the log normalised MEP ratio of A and B cues at cue offset (left) and probe onset (right). Dots represent individual participants; line represents best linear fit; shaded area represents 95% confidence interval; density distributions are represented on the top and right axes.

significance – BX accuracy was significantly correlated with the MEP ratio measure at cue offset but not probe onset (Figure S2, Supplementary Materials).

3.4. Successful versus unsuccessful inhibition

Finally, we examined whether the neurophysiological signatures of inhibition differed on non-target no-go trials when participants successfully versus unsuccessfully inhibited their response. To examine the effect of proactive inhibition on motor system activity, we examined MEPs during the cue offset and probe onset periods split based on whether participants *later* successfully versus unsuccessfully inhibited their response during the probe (see Fig. 5). At the cue offset, MEPs were generally low for successful inhibition of both AY and B trials. MEPs were higher when these trials were unsuccessfully inhibited and more so for B trials than AY trials. At the probe onset, MEPs were again low for successful inhibition of both AY and B trials, and MEPs were higher when these trials were unsuccessfully inhibited but more so for AY trials than B trials. The pattern of activity at cue offset is mirrored at probe onset such that larger MEP differences between successful and unsuccessful inhibition was seen for B trials at the cue offset and for AY trials at the probe onset.

Analysing the data as a 2 (Successful vs Unsuccessful) × 2 (AY vs B) × 2 (Cue offset vs Probe onset) factorial design, we observed a main effect of response outcome, such that unsuccessful inhibition trials had overall higher MEPs than successful inhibition trials, $F(1,13) = 7.24$, $p = 0.019$, $\eta_p^2 = 0.07$. No other main effects or interactions were significant. As explained in the Analysis subsection of the Methods, we follow-up these analyses with simple effects.

At cue offset, MEPs to the B cue were significantly higher when participants later made a commission error compared with when they successfully inhibited their response, $t(18) = 2.18$, $p = 0.043$, $d = 0.50$. This effect was specific to the B cue; MEPs to the A cue at this time point were not significantly different between successfully inhibited and unsuccessfully inhibited AY trials, $t(29) = 0.86$, $p = 0.397$, $d = 0.16$. That is, activity at the cue offset is more accurate in predicting success of B trials.

At probe onset, the pattern and statistics were mirrored for the trial type factor. MEPs after being presented the A cue were significantly higher when participants unsuccessfully cancelled their preparation to respond on AY trials compared with when they successfully inhibited their response, $t(29) = 2.24$, $p = 0.033$, $d = 0.41$. This effect was specific to AY trials; MEPs after being presented the B cue at this timepoint did not significantly differ between successfully and unsuccessfully inhibited B trials, $t(24) = 1.04$, $p = 0.307$, $d = 0.21$. That is, activity at the probe onset is more accurate in predicting success of AY trials.

To examine the effect of reactive inhibition on motor system activity, we split MEPs on AY trials during the probe according to whether participants successfully or unsuccessfully inhibited their response. Note, we included the probe onset (probe 0) timepoint in Fig. 6 for a point of reference but did not include it in the analysis since it was included in the proactive inhibition analysis (see Fig. 5). As shown in Fig. 6, MEPs remained relatively flat when trials were successfully inhibited but increased at around Probe 200 and remained high when trials were unsuccessfully inhibited. Overall, MEPs were significantly smaller on successful compared to unsuccessful inhibition trials, $F(1,19) = 19.20$, $p < 0.001$, $\eta_p^2 = 0.50$. This difference in MEP magnitude was significant at all timepoints with the largest effect size at Probe 200, $t(29) = 5.72$, $p < 0.001$, $d = 1.05$, compared with Probe 300, $t(20) = 2.99$, $p = 0.007$, $d = 0.65$, and Probe 100, $t(29) = 2.24$, $p = 0.033$, $d = 0.41$.

4. Discussion

Response inhibition research has often focused on reactive inhibition or used block- and task-level manipulations to investigate proactive inhibition by modifying reactive inhibition tasks (see Elchlepp et al., 2016). The current experiment studied proactive and reactive inhibition by adopting a two-step CPT commonly used in the cognitive control literature (e.g., Cohen et al., 1999; Servan-Schreiber et al., 1996). We measured corticospinal excitability with TMS during critical periods of the well-characterised DPX task to map inhibitory control processes reflected in the motor system. The pattern of performance on the DPX task was consistent with past research using other two-step CPTs.

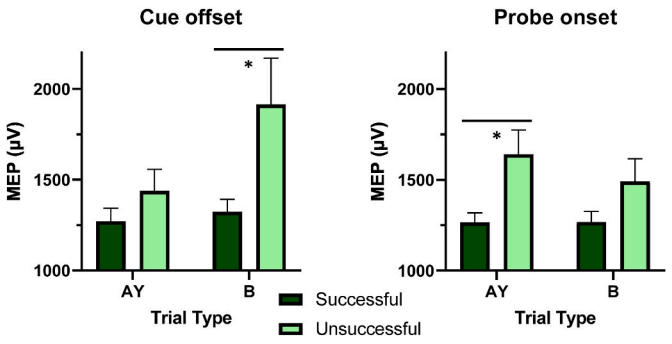

Fig. 5. Mean MEP for B and AY trials by successful versus unsuccessful response inhibition at cue offset (left) and probe onset (right). Error bars represent within participant standard errors. MEP = motor-evoked potential.

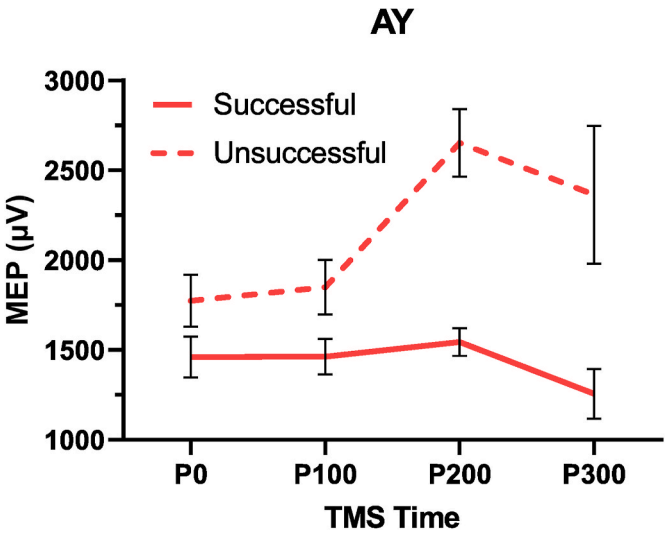

Fig. 6. Mean MEP for AY trials by successful versus unsuccessful response inhibition. Error bars represent within participant standard errors. P = probe; MEP = motor-evoked potential.

Combining TMS with the DPX task revealed several novel and interesting findings.

First, we found that MEPs provided a reliable index of proactive inhibition; differences in the amplitude of MEPs between conditions emerged early during the processing of the cue, despite no response being required at the time. Motor system activity at the offset of the B cue was lower than that of the A cue; and interestingly, more proactive individuals (based on PBI scores) showed greater suppression on B cues relative to A cues. Second, and as expected, we found that MEPs for AX trials rapidly increased during the probe as participants prepared to respond (Chen and Hallett, 1999; Davey et al., 1998; Leocani et al., 2000).

Third, we found that MEPs also provided an index of reactive inhibition and were sensitive to momentary changes in inhibitory processes during the probe. Motor system activity initially increased on AY trials, but was subsequently downregulated. Activity on BX and BY trials remained relatively low and flat. We predicted that BX trials might show a small increase relative to BY trials reflecting a form of conditioned motor preparation (e.g., Poole et al., 2018; Tran et al., 2019) due to the presence of the target X probe that is frequently paired with the target A cue and a go response. However, we did not find evidence to support this hypothesis in the current experiment.

Finally, we found the MEPs differed for successful and unsuccessful inhibition trials. Corticospinal excitability to the B cue at the *cue offset* period predicted whether participants would later successfully or unsuccessfully inhibit their response during the probe on BX and BY trials. In contrast, corticospinal excitability after the A cue at the *probe onset* period predicted whether participants would soon successfully or unsuccessfully inhibit their response during the probe on AY trials. Meanwhile, corticospinal excitability *during the probe* on AY trials was lower when participants successfully inhibited their response, and higher when participants unsuccessfully inhibited their response. We will consider each of these findings in turn and discuss their implications.

4.1. Corticospinal excitability during the cue

The neurophysiological results reveal that during the cue, proactive inhibition processes are already active, sufficiently so to influence downstream networks in the motor system that are responsible for variations in corticospinal excitability. This finding is consistent with past EEG research showing long latency (350–500 ms) positive amplitude differences in event-related potential (ERP) to the different control modes engaged during the A versus B cues (Javitt et al., 2000). However, finding amplitude differences in MEPs during the cue period were less of a guarantee than finding amplitude differences in ERPs. It is to be expected that different control modes would be engaged during the cue, but surprising that these control mechanisms—originating from the dlPFC and likely routing via the indirect pathway in the stopping network (Aron, 2011)—are already downregulating motor system activity even though participants are not required to make a response for some time, particularly since there is a cue period of 1000 ms and a cue-probe interval of 1000 ms. We selected the TMS timepoint to coincide with the offset of the cue since it provided the longest time to process the stimulation information by the cue. This timepoint ensured that any variations in MEP observed are not the result of reflexive and transient reactions to stimulus onset that are impulsive but quickly controlled (van Wouwe et al., 2009); rather participants have time to process the cue identity and use this information to plan their future task requirements. Therefore, we can conclude that fluctuations in MEP magnitude reflect differences in motor preparation and planning.

Our finding is consistent with previous research showing that corticospinal excitability is suppressed if the individual expects that they may need to stop (Claffey et al., 2010). However, this previous study used a bimanual response task in which stopping with one hand was confounded with responding with the other hand. Hence, differences in motor system activity due to the possibility of stopping could be partly or entirely due to interhemispheric inhibition of preparing an action with the contralateral responding hand. The present study used a unimanual go/no-go response task and avoids this issue. Additionally, our results show that proactive modulation of corticospinal excitability can occur sooner than has been previously tested. Of course, it is possible that the difference in excitability between A and B cues may be even greater if TMS was triggered during the cue, earlier than we have tested here. However, as discussed above, selecting the optimal timepoint to reveal this difference includes other considerations.

We also showed that the extent to which motor system activity to the B cue is downregulated at the cue offset is predicted by PBI across individuals (Fig. 4). Within individuals, it also predicts whether participants are able to successfully inhibit their response later during the probe (Fig. 5, left). Considered together, the results at the time of cue offset reveal a close correspondence between behavioural and neurophysiological inhibition, whereby preparing to stop occurs early, and the effectiveness with which early motor system activity is modulated relates to a commonly used behavioural index of proactive capacity and directly impacts on subsequent stopping success. In line with our individual differences result using the PBI, we expect that in populations with impaired proactive inhibition, such as in older adults or people with schizophrenia, MEPs during the cue can provide a reliable neural marker of proactive engagement. We hypothesise that in such populations, differences in motor system activity between A and B cues will be less pronounced compared to the patterns observed with healthy adults in this present study. In other words, we expect that preparatory inhibition during the B cue is a marker of healthy planning.

4.2. Corticospinal excitability during the probe

During the probe, MEPs increased rapidly for AX trials as participants prepared to respond. This rise in corticospinal excitability for AX trials is consistent with the activity of go trials in the maybe stop condition of the conditional stop signal task (Jahfari et al., 2010). The MEP increase in the current experiment appears steeper than that reported by Jahfari and colleagues, but this may be due to our inclusion of both 200 and 300 ms timepoints after the probe, whereas Jahfari and colleagues stopped at 200 ms. In contrast to AX trials, activity remained relatively flat for BX and BY trials as participants inhibited their responses. The MEPs for AY trials initially increased up to 200 ms after the onset of the probe and then decreased on the final timepoint 300 ms after onset. Based on the available timepoints, we can infer that peak activity on AY trials is between 100 and 300 ms; by the 300 ms time point, motor system activity is comparable to the levels of BX and BY trials. It would be interesting for future research to extend the timepoints beyond 300 ms and see whether MEPs for AY trials decrease even below the levels of BX and BY trials.

Splitting AY trials based on whether participants successfully or unsuccessfully inhibited their response (Fig. 6) provides further insight. The results show that the time between 100 and 300 ms after probe onset is a critical period for inhibitory control such that failing to engage in reactive inhibition leads to an increase in motor system activity between 100 and 200 ms and is maintained between 200 and 300 ms after the probe. However, this increase in motor system activity from 100 ms is not present on AY trials when participants successfully stopped their response. This finding suggests that if effective inhibitory control is not yet implemented by the 100–200 ms timepoint, it may be too late to correct and attempts to inhibit responding after this point may be ineffective at preventing errors. Otherwise, if it were possible to reactively stop later during the probe, MEPs for successful inhibition would show some increase followed by a decrease. The fact that motor system activity during the successful inhibition of AY trials remains relatively stable throughout the probe timepoints indicates that there were very few instances of successful stopping when motor system activity increased before being successfully downregulated (see also Tatz et al., 2021 for a similar pattern observed in the stop signal task). Although

past studies have investigated differences between successful and unsuccessful inhibition during reactive stopping (e.g., see Boehler et al., 2010), motor system activity has not been previously explored in this way with the temporal precision afforded by TMS.

Additionally, corticospinal excitability during AY trials at the probe onset (Fig. 5, right)—that is, immediately before the probe when participants had not yet processed the Y stimulus—informed whether participants would soon successfully or unsuccessfully cancel their preparation to respond. The information value of MEPs in predicting successful and unsuccessful trials at this (probe onset) timepoint was specific to AY trials and did not differ for B trials. Similarly, the information value of MEPs in predicting successful and unsuccessful trials at the cue offset timepoint was specific to B trials and did not differ for AY trials. These results present an interesting double dissociation between reactive versus proactive inhibition trials, and motor system activity early versus late during a trial. However, it should be noted that the three-way interaction between trial type, TMS time, and response outcome was not significant. We propose that the reduced sample size when comparing successful versus unsuccessful trials was a contributing factor in our failure to find a significant result. Nevertheless, these preliminary results provide a compelling avenue for further examination of proactive and reactive inhibition using TMS in combination with two-step CPTs.

There was little difference in motor system activity to BX and BY trials throughout the DPX task. Given the majority of X probes follow an A cue (≈87.5%) and are associated with making a response (on AX trials), we predicted that X probes following a B cue may also show some increase in motor system activity due to a learned association with the target response. Previous studies have found that go-associated cues can increase MEPs in the absence of requiring a response but can largely depend on the task context (Tran et al., 2019; Tran et al., 2021b). That is, the increased MEPs reflect a conditioned motor preparation that elevates motor system activity but remains below the threshold needed for responding. Critically, we do not think that the absence of a BX versus BY difference in corticospinal excitability reflects a passive state of inhibition to the B cue. The default state of the task is to respond, with AX comprising 70% of trials and A cues occurring on 80% of trials. One reason we may not have observed higher MEPs to BX compared to BY trials during the probe is that the participants actively inhibited any conditioned motor preparation proactively during the B cue. Given the observed behavioural differences between BX and BY trials on accuracies, but not in the neurophysiological differences with MEPs, our results suggest that the latter may be harder to detect, potentially due to greater trial-to-trial variability in corticospinal excitability compared to accuracy (since participants mostly responded or inhibited correctly). Although our sample of healthy adults did not show any MEP differences between BX and BY trials, specific populations known to have deficits in proactive control may show greater motor system activity during the probe on BX trials than on BY trials, in line with their documented behavioural deficits of having more BX errors.

4.3. Further considerations and conclusions

It should be noted that all the MEPs contributing to the figures and analyses are measurements taken before an actual response is made, and often in the absence of any response on the trial (in the case of successful AY, BX, and BY trials). The EMG signal is recorded from the right index finger that participants use to make a response. But in the case that a response is made when the TMS is triggered or if a muscle movement contaminates the EMG recording before the MEP, that TMS sample is excluded. The reported pattern of MEPs thus reveals the subthreshold modulation in motor system activity that is occurring during motor preparation and motor inhibition in the DPX task. Therefore, differences in motor system activity between the A cue and the B cue cannot be explained by participants prematurely responding to the A cue. Similarly, when MEPs are separated by successful and unsuccessful inhibition, the commission errors made on unsuccessful trials are made after the MEP is measured. Hence, differences in motor system activity between successful and unsuccessful trials cannot be accounted for by motor actions but reflect the engagement (e.g., active inhibition) or lack of engagement (e.g., failure of attention) with proactive control processes during the cue and reactive control processes during the probe.

Another interesting aspect of the neurophysiological data is the level of motor system activity displayed at probe onset (probe 0). The MEPs of cue A and B both converge to the same level of excitability, despite activity differences at the cue offset. It might be expected that any proactive inhibition to cue B (relative to cue A) would continue until the probe onset. However, the trend indicates that it is not cue B that is "released from inhibition" but that corticospinal excitability *reduces* for cue A. One possible explanation for the reduction in activity to cue A is that participants are engaging in a form of impulse control (e.g., Hasbroucq et al., 1997; Touge et al., 1998; Davranche et al., 2007; Duque and Ivry, 2009) to prevent premature responding to a highly probable X probe. An alternative explanation is that the motor system reduces excitability following an A cue, rather than sustaining it, to conserve metabolic energy when a response is not yet required (see Tran et al., 2021a or Tran and Livesey, 2021 for another possible explanation that is beyond the scope of this discussion on motor control).

An important feature of our DPX task, and indeed typical AX-CPTs, is that AX pairs comprise the majority of trials (approximately 70-10-10-10 for AX-AY-BX-BY). The pattern of corticospinal excitability we observed would likely differ if A trials were not overly represented or if AX and AY trials were equally frequent. Variations to the proportion of trials have been shown to affect both behaviour and neurophysiological measures using EEG (e.g., Dias et al., 2003). Therefore, our results most accurately reflect situations in which the tendency to make a response is prepotent.

The current experiment is the first to use TMS in combination with a two-step CPT, specifically the DPX task, to measure online fluctuations in motor system activity. One key advantage of adopting a task from the cognitive control literature and using it to study response inhibition, is the ability to apply well-validated measures, such as the PBI, to understand underlying processes during inhibitory control. By recording MEPs during the cue and probe periods, we were able to map changes in the control processes involved in proactive and reactive inhibition. We showed that during proactive inhibition, there are detectable downstream effects on the motor system even before a response needs to be initiated, and the extent of this modulation varies with individual differences in proactive behaviour. We showed that during reactive inhibition, motor system activity is difficult to downregulate after a certain point once it becomes a "runaway response". Critically, our findings indicate that response inhibition relies on preparing or engaging the inhibitory network as soon as possible because stopping success is likely determined much earlier than we had previously thought, emphasising the need for and importance of studying proactive inhibition.

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Credit author statement

DT: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Software; Supervision; Visualization; Writing - original draft; Writing - review & editing. IP: Conceptualization; Methodology; Writing - review & editing. RO: Software; Methodology; Writing - review & editing. EL: Conceptualization; Funding acquisition; Methodology; Resources; Supervision; Writing - review & editing.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuropsychologia.2022.108348.

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