

Motor Memory: Revealing Conditioned Action Tendencies Using Transcranial Magnetic Stimulation

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Abstract

■ *Action tendencies* can be elicited by motivationally salient stimuli (e.g., appetitive rewards) or objects that support utilization behaviors. These action tendencies can benefit behavioral performance through speeded RTs in response tasks and improve detection accuracy in attentional capture tasks. However, action tendencies can be counterproductive when goals change (e.g., refraining from junk foods or abstaining from alcohol). Maintaining control over cue-elicited action tendencies is therefore critical for successful behavior modification. To better understand this relationship, we used transcranial magnetic stimulation to investigate the neural signatures of action tendencies in the presence of previously trained response cues. Participants were presented with a continuous letter stream and instructed to respond quickly to two target letters using two different response keys. Following this

training phase, the target letters were embedded in a new task (test phase), and we applied transcranial magnetic stimulation to the motor cortex and measured motor evoked potentials as an index of corticospinal excitability (CSE). We found that CSE could be potentiated by a former response cue trained within a single experimental session, even when participants were instructed to withhold responses during the test phase. Critically, attention to the previously trained response cue was required to elicit the primed modulation in CSE, and successful control of this activity was accompanied by CSE suppression. These findings suggest that well-trained response cues can come to prime a *conditioned action tendency* and provide a model for understanding how the implementation of cognitive control can override action automaticity. ■

INTRODUCTION

Many cues in our environment are associated with a specific action. The sound of a pedestrian traffic signal initiates walking, the stop sign at a road intersection initiates braking, and even food-associated cues can initiate approach behaviors (see Petrovich, 2011). These learned cue–response associations help with action preparation and selection in everyday life, but they can also lead to unwanted behaviors when conflicting information is presented or when cognitive control fails. Inattention can result in miscued walking at the sound of an adjacent pedestrian traffic signal, distraction can result in mistimed stopping at an intersection, and failed impulse control can result in eating junk foods while on a diet. However, despite the ubiquity of action errors in everyday life, a comprehensive model for understanding how they occur is still lacking.

One method for studying motor preparation and control is to use transcranial magnetic stimulation (TMS). Modulation of activity in the motor system can be measured by applying TMS over the primary motor cortex while EMG is recorded from a muscle in the contra-

lateral hand. The EMG activity produced by the TMS, a motor evoked potential (MEP), provides an index of the corticospinal excitability (CSE) of the hand representation in the motor system. Using TMS in this way to map changes in cognitive and motor processes (Bestmann & Duque, 2016), previous studies have found that “graspable” objects supporting utilization behaviors (e.g., mugs) elicit larger MEPs compared with “nongrasable” objects (McNair, Behrens, & Harris, 2017; Cardellicchio, Sinigaglia, & Costantini, 2011; see also Freeman, Itthipuripat, & Aron, 2016; Franca et al., 2012; Makris, Hadar, & Yarrow, 2011; Grafton, Fadiga, Arbib, & Rizzolatti, 1997). Similarly, other research has shown that left and right pointing arrows can affect MEPs and that the modulations of CSE by these prepotent stimuli were even present when the arrows were presented as a masked prime preceding a target in a bimanual choice RT task (Verleger, Kötter, Jaśkowski, Sprenger, & Siebner, 2006). Specifically, MEPs were larger for the responding hand compared with the nonresponding hand, and this effect was greater when the target was preceded by a congruent arrow compared with an incongruent or neutral prime.

In another study using a bimanual response task, TMS was used to probe action tendencies before the execution of a response where participants were manipulated

to be truthful or deceitful (Hadar, Makris, & Yarrow, 2012). Unsurprisingly, when participants were instructed to tell the truth, MEPs of the nonresponding (deceitful) finger were smaller than MEPs of the responding (truthful) finger. However, when instructed to lie, MEPs of the nonresponding (truthful) finger were greater than MEPs of the responding (deceitful) finger, suggesting that the objectively correct motor response was automatically activated. Notably, this effect was still present when participants made a verbal response that had been associated with a finger-specific motor action. This result reveals that verbal–motor associations can be strong enough to trigger MEPs in the associated muscle and provides preliminary evidence that trained cues may come to involuntarily activate the motor system in a similar manner.

Stimuli that predict the availability of appetitive or monetary rewards have also been shown to elicit larger MEPs than neutral cues (Freeman, Razhas, & Aron, 2014; Klein, Olivier, & Duque, 2012; see also, Mooshagian, Keisler, Zimmermann, Schweickert, & Wassermann, 2015; Vassena, Cobbaert, Andres, Fias, & Verguts, 2015; Thabit et al., 2011; Kapogiannis, Campion, Grafman, & Wassermann, 2008). For example, researchers have used TMS in combination with a cue–target delay paradigm to investigate the effect of CSE on reward anticipation (Bundt, Abrahamse, Braem, Brass, & Notebaert, 2016). In this task, there was a 1000-msec window between the onset of a warning cue indicating whether or not reward could be expected for a fast and accurate response to a target cue. Compared with a no-reward warning cue, the reward warning cue produced greater CSE activity early, but this activity decreased over time. This initial reward-related increase in CSE was proposed to reflect a cue-elicited tendency to perform approach/appetitive behaviors toward the reward-predicting stimulus, which became suppressed over time due to impulse control for avoiding premature responses. In line with this finding, there is also evidence that motivational factors based on cue valence can modulate CSE. Appetitive cues were found to increase CSE, and aversive cues decreased CSE (Chiu, Cools, & Aron, 2014; see also Klein-Flügge & Bestmann, 2012; Gupta & Aron, 2011). Furthermore, these same motivational cues were shown to bias behavior and increase action errors in a go/no-go task with appetitive cues biasing responding, whereas aversive cues biased withholding a response.

Together, previous TMS studies investigating motor system activity toward prepotent and rewarding stimuli reveal how MEPs can be used to study action tendencies and suggest that the mere presence of certain stimuli in our environment is sufficient to prepare the motor system for approach behavior. However, much is still unknown about the mechanisms through which these motor activation effects emerge or the conditions that modulate this evoked activity. We sought to address these outstanding questions while also examining the hemispheric specificity of such effects, given recent

findings of hemispheric asymmetries in the lead up to motor execution (Poole, Mather, Livesey, Harris, & Harris, 2018; Klein, Duque, Labruna, & Ivry, 2016). Elucidating the mechanism and conditions that underlie cue-elicited motor activation will enrich current models of cognitive control. Therefore, to better understand how and why action errors occur, across four experiments, we investigated the interactions between “motor priming” of action tendencies and competing task demands that required various cognitive control processes. We defined motor priming as an externally triggered or cue-elicited effect that ultimately modulates activity—excitatory or inhibitory—in the motor system as indexed by MEPs. In this study, we examined whether an abstract cue trained to be associated with a specific response would come to elicit a “conditioned” action tendency. That is, will merely presenting a trained cue in the absence of any response requirements prime the motor system, in the form of increased CSE, compared with presentations of an untrained cue? Additionally, we explored how such motor priming effects are modulated by competing tasks demands and how selective such motor priming effects are to the trained muscle and motor hemisphere. To investigate the former question, we embedded the trained cues within three different tasks that varied how attention was allocated to the trained cues and their requirement to engage in action selection (Figure 1). To investigate the latter question, we trained a nondominant hand and dominant hand response and measured activity in the nondominant or dominant motor hemisphere.

MATERIAL AND METHODS

Design

In four experiments, participants were first trained to make speeded responses to two critical letters in a rapid serial visual presentation stream; one letter signaling a left-handed response, and the other signaling a right-handed response. Following the training phase, participants performed a new task in a rapid serial visual presentation stream (test phase) in which they no longer responded manually to the critical letters. Instead, they had to count the number of times the critical letters appeared (Experiment 1, Figure 1C), count the number of times two new letters appeared (Experiment 2, Figure 1D), or respond manually to two different letters (Experiment 3, Figure 1E). Although participants were engaged in these tasks, TMS was triggered during the presentation of the critical letters (i.e., the previously trained response cues). The first three experiments conformed to a $2 \times (2) \times (2)$ design. The first, between-participant factor was the hand from which MEPs were recorded (dominant vs. nondominant hand MEP), which was randomly allocated when participants arrived at the lab. The second, within-participant factor was the

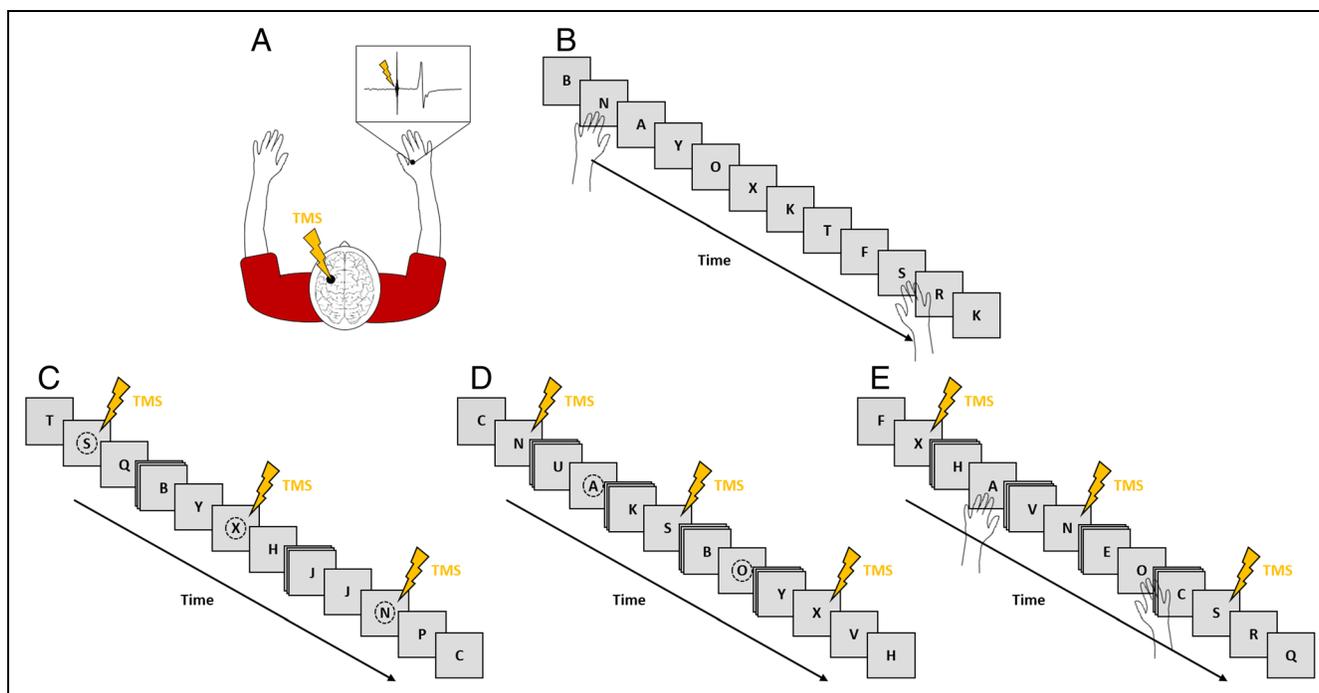


Figure 1. Schematic of the experimental setup, training task, and test task. (A) As illustrated, TMS was applied over the nondominant (or dominant) primary motor cortex and EMG was recorded from the first dorsal interossei muscle of the index finger of the contralateral hand. (B) The training task was the same for all four experiments and was used to establish a cue–response association with the dominant (e.g., letter S) and nondominant hands (e.g., letter N). The test task differed across experiments: (C) Experiment 1 had a letter counting task in which the trained response cues were still relevant (count S, N, and X), (D) Experiment 2 had a letter counting task in which the trained response cues were no longer relevant (count A and O), and (E) Experiment 3 had an action selection task in which the previous response cues were no longer relevant (respond to A and O). Experiment 4 had two tests (the counting task used in Experiment 1 and the response task used in Experiment 3) separated by a retraining phase that was identical to the training phase. Letter stimuli were presented on screen for 500 msec, and single pulse TMS was triggered 300 msec after the onset of a target letter presentation. Circles around the letters in C and D refer to the instructed letters that participants were required to count during the test phase; hand images in B and E identify letters that participants responded to with a key press.

trained critical letters (dominant vs. nondominant hand response letter). The third, within-participant factor was the timing of the TMS pulse during the test phase (200 vs. 300 msec SOA). The results from the main article report the findings from the 300-msec time point, and the data for the 200-msec time point can be found in the supplementary materials.¹

In Experiment 4, we sought to replicate the findings from Experiments 1 and 3 within a single experiment, focusing only on the dominant hand MEP at the 300-msec SOA. Following the training phase, participants performed the test phase from Experiment 1, had retraining, and then performed the test phase from Experiment 3 (with test order counterbalanced across participants). Experiment 4 conformed to a $(2) \times (2)$ design. The first, within-participant factor was the trained critical letters (dominant vs. nondominant hand response letter). The second, within-participant factor was task during the test phases (count critical letter vs. respond to new letters).

Participants

Participants were undergraduate students from The University of Sydney who received partial course credit

in exchange for their participation or were remunerated for their time. Each participant completed a TMS safety screening and provided informed consent before commencing the experiment. All procedures were approved by the human research ethics committee of The University of Sydney.

Experiment 1

Seventy-six participants were recruited for Experiment 1. Two participants were excluded because a reliable motor twitch could not be elicited. Three participants were excluded because problems with the equipment prevented us from collecting a complete data set. Three participants were excluded for having MEPs $< 50 \mu\text{V}$ on more than 50% of the total 120 TMS trials, typically due to a participant's head frequently moving away from the coil. An additional two participants were excluded for having more than 50% missing trials from two or more of the six conditions. Seven participants were excluded for having poor performance on the training and test task: training accuracy $\leq 65\%$ ($M = 74.98$, $SD = 10.94$) and test accuracy $\leq 50\%$ ($M = 64.31$, $SD = 18.52$); four were from the dominant hand group, and three were from the

nondominant hand group. Training and test accuracy exclusions were used as manipulation checks to ensure that participants were effectively trained on the cue–response association and that they attended to the appropriate stimuli during test. Four participants were excluded for having mean normalized MEPs greater than 3 *SDs* from the condition mean (Freeman et al., 2014); two were from the dominant hand group, and two were from the nondominant hand group. Statistical analyses were run on the remaining 55 participants (41 women, age = 19.05 (2.35) years).

Experiment 2

Seventy-two participants were recruited for Experiment 2. Three participants were excluded because a reliable motor twitch could not be elicited. Five participants were excluded for having incomplete data due to equipment issues. Five participants were excluded for having MEPs <50 μV on more than 50% of TMS trials. An additional two participants were excluded for having more than 50% missing trials from two or more of the six conditions. No participants were excluded for having poor performance on combined training ($\leq 65\%$, $M = 71.57$, $SD = 13.33$) and test ($\leq 50\%$, $M = 83.52$, $SD = 13.36$) accuracy. Three participants were excluded for having mean normalized MEPs greater than 3 *SDs* from the condition mean; two were from the dominant hand group, and one was from the nondominant hand group. Statistical analyses were run on the remaining 54 participants (37 female, age = 22.83 (6.75) years).

Experiment 3

Seventy-seven participants were recruited for Experiment 3. Two participants were excluded because a reliable motor twitch could not be elicited. Three participants were excluded for having incomplete data due to equipment issues. Two participants did not finish the experiment, and one participant was asked to discontinue due to poor task engagement during training. Nine participants were excluded for having MEPs <50 μV on more than 50% of TMS trials. A further four participants were excluded for having more than 50% missing trials from two or more of the six conditions. One participant was excluded for continuing to perform the training task during the test phase that had a different task instruction (i.e., they continued to respond on 78/80 of the trained cue trials). One participant from the dominant hand group was excluded for having poor performance on combined training ($\leq 65\%$, $M = 70.57$, $SD = 12.69$) and test ($\leq 50\%$, $M = 74.82$, $SD = 13.11$) accuracy. Three participants from the dominant hand group were excluded for having mean normalized MEPs greater than 3 *SDs* from the condition mean. Statistical analyses were run on the remaining 51 participants (29 female, age = 21.00 (4.21) years).

Experiment 4

Forty participants were recruited for Experiment 4. One participant was excluded because they had participated in one of the previous experiments. Four participants had their data excluded from both test phases for having poor performance during both the training ($\leq 65\%$, $M = 74.75$, $SD = 11.49$) and retraining phases ($\leq 65\%$, $M = 77.39$, $SD = 11.26$). Four participants were excluded from the count test phase, and four participants were excluded from the response test phase for having MEPs <50 μV on more than 50% of TMS trials; two of these participants were the same (i.e., excluded from both test phases). A further three participants were excluded for having poor performance on the count test phase ($\leq 50\%$, $M = 78.46$, $SD = 19.67$), and two participants were excluded on the response test phase ($\leq 50\%$, $M = 68.21$, $SD = 15.23$). Three participants were excluded for having mean normalized MEPs greater than 3 *SDs* from the condition mean; one was from count test phase, and two were from the response test phase. Statistical analyses were run on the remaining 27 participants from the count test phase (16 female, age = 24.00 (5.22) years) and 27 participants from the response test phase (17 female, age = 23.66 (5.09) years). Of these, 22 participants had complete data and were included in the analyses of both test phases.

Methods

Apparatus and Stimuli

The experiment was run on a personal computer connected to a 17-in. CRT monitor (1280 \times 1024 pixel, 85 Hz refresh rate) at a viewing distance of approximately 75 cm. PsychoPy (Version 1.83.03) was used to present stimuli and collect response data. Visual stimuli were capital letters presented at the center of the screen in black text against a white background. The letters fit to a 100 \times 100 pixel space and subtended a visual angle of approximately 2°.

EMG and TMS

Surface EMG recorded the MEP activity from the first dorsal interosseus (FDI) muscle of either the dominant or nondominant hand, depending on group allocation. In preparation for electrode placement, the skin was cleaned with a small sponge and wiped with 70% v/v isopropyl alcohol swab. Two 10-mm diameter Ag/AgCl electrodes were placed in a belly-tendon arrangement over the FDI muscle along with the ground electrode placed over the ulnar styloid process of the wrist. EMG activity was recorded from 200 msec prestimulation to 100 msec post-stimulation using PowerLab 26T DAQ (ADInstruments). This signal was digitally converted (sampling rate: 4 kHz, bandpass filter: 0.5 Hz to 2 kHz, mains filter: 50 Hz, and anti-aliasing) and stored using LabChart software (Version 8, ADInstruments) for offline processing.

TMS was administered using a Magstim 200² and Rapid² stimulator for Experiment 1, a Rapid² stimulator for Experiments 2 and 3, and a Magstim 200² stimulator for Experiment 4. All experiments used a 70-mm figure-eight coil (Magstim) locked in position with an adjustable arm (Manfrotto, Italy) that was secured onto a custom-made frame on the participant's chair. The position of the coil was checked after every block and repositioned if the participant moved their head. Participants wore an elastic cap marked with the 10/20 EEG electrode locations and rested their head on a custom chin and forehead rest. The coil was held tangentially to the scalp with the handle orientated 45° from the midline. The location of the motor cortex "hotspot" was determined starting from a spot 5 cm lateral and 1 cm anterior to Cz, the coil was moved around until the maximal MEP was elicited in the FDI. Resting motor threshold was determined by finding the lowest stimulation intensity that produced a minimum of 100 μ V in 5 of 10 consecutive trials. The same thresholding procedure was used across both the Magstim 200² and the Rapid². The average stimulator intensity for Experiment 1 was 64.70% ($n = 25$, Rapid²) and 43.34% ($n = 30$, Magstim 200²), Experiment 2 was 68.64% (Rapid²), Experiment 3 was 67.76% (Rapid²), and Experiment 4 was 44.18% (Magstim 200²). The difference in averaged pulse intensity between the two stimulators is due to differences in power output and pulse characteristics, which affects the size of the MEP (Delvendahl et al., 2014). Two stimulators were used in Experiment 1 due to technical issues; however, an ANOVA including Stimulator as a factor did not affect the results or return any significant interactions with the other factors.

Experimental Procedure

The experiment consisted of two types of phases: training and test. In Experiments 1–3, the training and test phases lasted approximately 40 and 20 min, respectively; the total testing session (including briefing, setup, and debriefing) for these experiments lasted approximately 90 min for each participant. In Experiment 4, the phases lasted approximately 40 min (training), 15 min (Test 1), 20 min (retraining), and 15 min (Test 2); the total testing session lasted approximately 120 min for each participant. The EMG setup and TMS procedures were carried out before the training phase. During all phases, participants were presented with letter stimuli in a serial order, each with an SOA of 500 msec and an ISI of 0 msec. Letters were randomly selected with the exception that there were no immediate repetitions, and presentations of the critical letters (N, S, and X) were carefully counterbalanced.

Training. All four experiments began with the same training phase (Figure 1B) with three designated critical letters (N, S, and X). One critical letter (e.g., N) was assigned as a left response cue, another (e.g., S) as a right

response cue, and the final critical letter (X) was a control stimulus matched for the frequency of presentation throughout the training phase. The control letter was used to normalize MEPs for the left and right response cue letters. The allocation of these letters to response cues was counterbalanced using a 3×3 Latin square design, and allocation was assigned when participants arrived at the lab. Participants were instructed to press the Left Ctrl key using the left index finger as soon as they saw the left letter cue, to press the Right Enter key using their right index finger as soon as they saw the right letter cue, and to rest their fingers on these keys throughout training, with their hands relaxed and flat on the table. Participants were allowed a 600-msec time window, from the onset of the letter, to respond before receiving a buzzing sound. We used a 600-msec timeout to encourage speeded, imperative responses from participants but recognized that this timeout in a choice RT task would be difficult for some participants. Therefore, responses made after this time were still recorded to assist with performance measure checks. The same buzzing sound was also used as feedback when an incorrect key was pressed. A chiming sound provided feedback when the correct key was pressed. One trial sequence consisted of 10–14 letters, with five trials in one block. Each block contained two trials with a left cue letter in the sequence, two trials with a right cue, and one trial with no response cues in the sequence; these five trials were blocked in a random order. Within each block, the control letter also appeared twice, matching the number of presentations of the left and right cues; all other letters were filler. There were 10 blocks in one session, and six sessions in the training phase with each session separated by a self-timed break (apart from these breaks, all letters, trials, and blocks were presented as a seamless sequence of serially presented letters). An additional buffer trial with no response cue occurred at the beginning of each session to settle the participants into the response task. The training phase contained 120 left and 120 right response cue trials.

Retraining. The retraining phase used in Experiment 4 between the two test phases helped participants to reacquire the cue–response association with the critical letters after having performed a different task during the first test phase. The retraining phase was identical to the training phase, except it was half as long; there were three sessions separated by a self-timed break and 60 left and 60 right response cue trials.

Experiment 1. During the Experiment 1 test phase (Figure 1C), participants were instructed to withhold responding to the trained response cues (e.g., N and S). Instead, they were asked to count the number of times the letters N, S, and X appeared while resting their fingers on the trained response keys with their hands relaxed and flat on the table. The trial structure during training was maintained at test, with one trial sequence

consisting of 10–14 letters. Each block contained 12 TMS trials: four trials with a left-trained letter cue in the sequence, four trials with a right-trained letter cue in the sequence, and four trials with a control letter in the sequence (i.e., four trials containing an N, S, and X). Half of the TMS trials (two of each letter stimulus type) triggered a single pulse 200 msec after the onset of the letter, and half of TMS trials triggered a single pulse at 300 msec. The results presented in the main article are for the 300-msec triggers. The results for the 200-msec triggers did not reveal any interesting pattern, likely because they were too early given the timing of responses; we have therefore included the 200-msec data in the supplementary materials.¹ Each block also contained five non-TMS trials: four filler trials (for which there was a 75% chance that one of the three critical letters appeared, each with equal probability) and one buffer trial. Trials were randomly ordered within a block except for the buffer trial, which always occurred at the beginning. There were 10 blocks in the test phase with a count check question at the end of each block. For the count question, participants were asked whether the number of N, S, and X letters that appeared in the previous block totaled an odd number (press the Left Ctrl key) or an even number (press the Right Enter key). A two-alternative question was used so that participants could continue to rest their index fingers on the previously trained left and right response keys, maximizing the transfer of any conditioned modulation in CSE from the training phase. This instruction also served to help participants keep their head still for the TMS procedure as they did not need to move their head when entering an answer. The additional four non-TMS filler trials were included to vary the correct answer to the count question; upon answering the question, participants were provided with feedback on whether their answer was correct or incorrect and instructed to reset their count.

Experiment 2. The test phase for Experiment 2 (Figure 1D) was identical to that of Experiment 1, except participants were asked to count the number of times the letters A and O appeared while withholding responses to the trained response cues (e.g., N and S). Each block contained 12 TMS trials and 5 non-TMS trials (four fillers and one buffer), as in Experiment 1 (NB: Each trial sequence consisted of 10–14 letters and TMS occurred during N, S, and X letters). The four filler trials in this experiment did not contain any critical events but were included to maintain the same trial structure and TMS trigger spacing across Experiments 1–4. With the exception of the critical letters, all letters (including A and O) were selected with equal probability to be fillers. For the count question at the end of each block, participants were asked whether there were more (or as many) presentations of A than O letters (press the Left Ctrl key) or more of O than A letters (press the Right Enter key). Upon answering the question, participants were provided with feedback on

whether their answer was correct and instructed to reset their count. If their answer was incorrect, they were provided with the correct answer and the difference value.

Experiment 3. The test phase for Experiment 3 (Figure 1E) was identical to the previous experiments, except participants were asked to respond to the letters A and O while withholding responses to the trained response cues (e.g., N and S). Participants were instructed to press the Left Ctrl key using the left index finger as soon as they saw the letter A and the Right Enter key using their right index finger as soon as they saw the letter O. Each block contained 12 TMS trials (for the N, S, and X letters) and 5 non-TMS trials (four fillers and one buffer) with each trial consisting of 10–14 letters, as in Experiments 1 and 2. The four filler trials composed of two trials containing the letter A in the sequence and two trials containing the letter O in the sequence. The letters A and O did not otherwise appear during a TMS trial to prevent any potential response contamination to the MEPs. Participants received auditory feedback on the response trials as they did during training.

Experiment 4. The count and response test phases for Experiment 4 were identical to that used in Experiments 1 and 3, respectively, except with fewer TMS trials and an improved method of inputting answers for the count task. Each block contained six TMS trials: two trials with a left-trained letter cue in the sequence, two trials with a right-trained letter cue in the sequence, and two trials with a control letter in the sequence (i.e., two trials containing an N, S, and X). On all of the TMS trials, a single pulse was triggered at 300 msec. For the count question, participants were asked to select the total number of N, S, and X letters they counted using a number scale ranging from 1 to 15. A marker appeared in a random location between 5 and 11, and participants could press the Left Ctrl key to move the marker left or the Right Enter key to move the marker right. To input their selected answer, participants pressed the space key; they were then provided with feedback on whether their answer was correct or incorrect and instructed to reset their count. This new method of inputting answers still allowed participants to rest their index fingers on the previously trained left and right response keys but also provided a quantification on the accuracy of the count beyond the odd versus even judgment used in Experiment 1. Filler trials were used in the same way as Experiment 1 to vary the total number of critical letters in each block (so the count answer was not always six). The two test phases were separated by the retraining phase, and test order was counterbalanced with participants randomly allocated when they arrived at the lab.

Data Analysis

Custom Python software was used for screening and selecting MEP data. Each trial was visually inspected to

exclude atypical MEP waveforms and pre-TMS movement artifacts in the EMG signal ($>50 \mu\text{V}$). MEP amplitudes were defined as the highest to lowest point of activity before returning to baseline. Participants were excluded for having MEPs $<50 \mu\text{V}$ on more than 50% of the total TMS trials (number of participants excluded are specified in the Participants subsection). For the remaining participants, any MEP less than $25 \mu\text{V}$ was treated as a mis-trigger and excluded from the analysis. We used a $25\text{-}\mu\text{V}$ instead of a $50\text{-}\mu\text{V}$ criterion for the exclusion of specific trials since we were investigating conditions that might give rise to inhibition and did not want to potentially remove any legitimately small MEPs. The mean MEP amplitudes for each trained response cue (N and S) were normalized to a mean MEP amplitude of a control stimulus (X) before a log transformation. Test trials in which participants accidentally made a response (false alarms) to the previously trained response cue (target) letters were removed from the analysis to avoid artificial inflation of MEPs. False alarms were rare and only occurred during Experiment 3 ($M = 3.24\%$ of trials, $SD = 3.48$) and the response test phase of Experiment 4 ($M = 4.26\%$ of trials, $SD = 6.19$).

RESULTS

Training (and Retraining) Phase (Experiments 1–4)

The training phase was the same across all four experiments. Participants made speeded responses to two target letters (N and S) that appeared within a continuous letter stream. One letter indicated an imperative nondominant hand response and the other an imperative dominant hand response. Accuracy (calculated with omission errors included in the denominator) on the cue–response training task was high across all experiments, particularly when including late responses made after the 600-msec timeout (see Table 1).

Experiment 1 Test Phase

Following the training phase, participants performed a passive counting task (test phase) where they were instructed to withhold responding to the two target letters

and instead silently count the total number of N, S, and X letters that appeared. During the presentation of these three letters, TMS was triggered to measure CSE to the left trained response letter, the right trained response letter, and an untrained control letter. The primary aim of Experiment 1 was to find evidence for a motor priming effect to the trained response cues (N and S) while engaged in a nonresponse (counting) task. A secondary aim of Experiment 1 was to explore how such motor priming effects are differentiated between the dominant and nondominant hands and motor hemispheres. An ANOVA with a between-participant factor of MEP hand (MEPs measured from the dominant hand in one group vs. the nondominant hand in the other) and a within-participant factor of Response letter (letters cued participants to respond with their dominant vs. nondominant hand) revealed that there was no significant effect of MEP hand, $F(1, 53) = 1.06, p = .308, \eta_p^2 = .020$, a marginally significant effect of Response letter, $F(1, 53) = 3.20, p = .079, \eta_p^2 = .057$, and a significant interaction, $F(1, 53) = 4.69, p = .035, \eta_p^2 = .081$. Follow-up comparisons showed that, for the nondominant MEP group, there was a marginal increase in CSE above baseline when collapsed across response letter (comparing the log-normalized MEP to 0), $t(26) = 1.71, p = .095, d = 0.231$. For the dominant MEP group, there was a significant difference in CSE between the response letters, $t(27) = 2.70, p = .012, d = 0.582$, with the dominant response letter tending toward an increase above baseline, $t(27) = 1.50, p = .145, d = 0.284$, and the nondominant response letter tending toward a decrease below baseline, $t(27) = 1.60, p = .120, d = 0.303$ (Figure 2A). These results reveal that motor system priming within the nondominant hemisphere was activated in a cue-nonspecific manner, showing a generalized increase in activity following presentations of either response letter. However, motor system priming within the dominant hemisphere is activated in a cue-specific manner.

Experiment 2 Test Phase

Following the same training phase used for Experiment 1, participants performed a counting task where they were

Table 1. Mean (*SD*) Accuracy and RT for the Training Task for Experiments 1–4

	<i>On Time (Before 600 msec Timeout)</i>		<i>All Responses</i>	
	<i>Accuracy (%)</i>	<i>RT (msec)</i>	<i>Accuracy (%)</i>	<i>RT (msec)</i>
Experiment 1	74.98 (10.94)	482.09 (22.54)	87.75 (6.14)	510.88 (34.10)
Experiment 2	71.57 (13.33)	486.05 (16.96)	86.56 (7.58)	519.62 (36.52)
Experiment 3	70.57 (12.69)	485.31 (20.45)	84.42 (8.36)	517.19 (32.67)
Experiment 4 (training)	74.75 (11.49)	479.10 (19.98)	87.85 (7.01)	508.62 (30.56)
Experiment 4 (retraining)	77.39 (11.26)	485.58 (25.69)	87.44 (8.05)	505.76 (32.18)

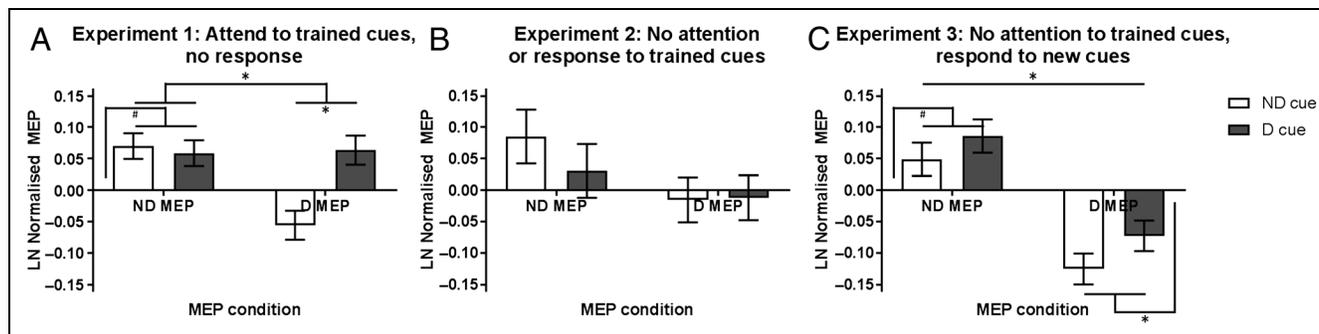


Figure 2. Log-normalized MEPs as a function of MEP recorded hand (ND [nondominant] MEP, D [dominant] MEP) and trained response cue hand (ND cue, D cue) for Experiments 1–3. MEPs were normalized relative to a neutral control letter (e.g., X). Error bars represent within-participant standard errors (Cousineau, 2005) for the response cue by MEP hand condition. * $p < .05$; # $p < .10$.

instructed to silently count the number of times the letters A and O appeared. Experiment 2 aimed to examine how the motor priming effects observed in Experiment 1 would be affected when attention was directed away from the trained response cues (N and S) during a nonresponse (counting) task. An ANOVA with the factors of MEP hand (dominant vs. nondominant) and Response letter (dominant vs. nondominant) revealed no significant effects of MEP hand, $F(1, 52) = 1.20, p = .278, \eta_p^2 = .023$, Response letter, or interaction ($F_s < 1$). These results show that the cue-specific priming pattern in the dominant hemisphere observed in Experiment 1 was a product of selective attention directed toward the trained cues during the counting task. Similarly, the cue-nonspecific priming pattern in the nondominant hemisphere observed in Experiment 1 was not reliably observed, with only a weak increase in CSE to both dominant and nondominant trained response letters, $t(25) = 1.29, p = .201, d = 0.180$ (Figure 2B).

Experiment 3 Test Phase

Following the same training phase used in the previous experiments, participants stopped responding to the trained response cues (N and S) and instead made speeded responses to two new letters, A and O. Experiment 3 aimed to examine how motor priming to the trained cues are affected by engaging in an action selection task that required a new cue–response mapping. An ANOVA with the factors of MEP hand (dominant vs. nondominant) and Response letter (dominant vs. nondominant) revealed a significant effect of MEP hand, $F(1, 49) = 10.01, p = .003, \eta_p^2 = .170$, but no significant effect of Response letter, $F(1, 49) = 1.48, p = .229, \eta_p^2 = .029$, or interaction ($F < 1$). We replicated the cue-nonspecific priming pattern in the nondominant hemisphere observed in Experiment 1, $t(25) = 2.00, p = .051, d = 0.277$. In Experiment 3, there was also a cue-nonspecific pattern of CSE suppression in the dominant hemisphere, $t(24) = 3.33, p = .002, d = 0.471$ (Figure 2C). These results show that, in an active response task where participants must inhibit responses to trained cues while preparing responses

to new cues, successful performance is accompanied by motor suppression to the trained cues.

Experiment 4 Test Phase

Following the same training phase used in the previous experiments, participants stopped responding to the trained response cues (N and S) and instead performed the cue-relevant counting task from the Experiment 1 test phase and the response task to new letters from the Experiment 3 test phase. Experiment 4 aimed to replicate the dominant hand MEP findings from Experiments 1 and 3 within a single experiment. Analyzing Experiment 4 as a full factorial design² with Task (count vs. response) and Response letter (dominant vs. nondominant) revealed a significant effect of Task, $F(1, 21) = 6.93, p = .016, \eta_p^2 = .248$, and Response letter, $F(1, 21) = 5.37, p = .031, \eta_p^2 = .204$, but no significant interaction ($F < 1$). The main effect of Task confirmed that the pattern of CSE differs between the two types of task participants were engaged in while withholding responses to the previously trained target letters. The main effect of Response letter is largely driven by the differences in CSE on the count task (Figure 3).

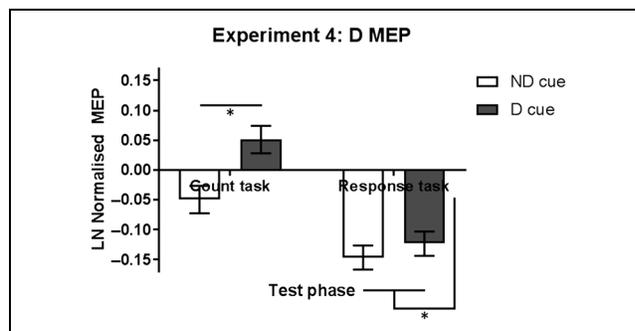


Figure 3. Log-normalized MEPs for Experiment 4 recorded from the dominant hand as a function of trained response cue hand (ND [nondominant] cue, D [dominant] cue). MEPs were normalized relative to a neutral control letter (e.g., X) for the count task (left; $n = 27$) and response task (right; $n = 27$). Error bars represent within-participant standard errors (Cousineau, 2005) for the response cue by test task. * $p < .05$.

The pattern of results for the count task (when participants counted the previously trained cues) replicates what we had observed in the same condition for Experiment 1 (see two bars, marked as D MEP, on right half of Figure 2A). In the current experiment, there was a significant difference in CSE between the response letters, $t(26) = 2.18$, $p = .038$, $d = 0.667$. Follow-up single-sample t tests showed that MEPs during the dominant response letter tended toward an increase above baseline, $t(26) = 1.80$, $p = .084$, $d = 0.346$, and during the nondominant response letter tended toward a decrease below baseline, $t(26) = 1.68$, $p = .106$, $d = 0.322$. Pooling the data from Experiments 1 and 4, there was a significant difference in CSE between the response letters, $t(54) = 3.48$, $p = .001$, $d = 0.616$ (replication $BF_{10} = 6.79^3$; Ly, Etz, Marsman, & Wagenmakers, 2018), as well as a significant increase above baseline for the dominant response letter, $t(54) = 2.25$, $p = .028$, $d = 0.304$ (replication $BF_{10} = 2.72$) and a significant decrease below baseline for the nondominant response letter, $t(54) = 2.32$, $p = .024$, $d = 0.313$ (replication $BF_{10} = 2.75$).

We also replicated the pattern of results for the response task (when participants responded to two new letters). There was a cue-nonspecific pattern of CSE suppression in the dominant hemisphere averaging across response letter, $t(26) = 4.00$, $p < .001$, $d = 0.770$. Pooling the data from Experiments 3 and 4, there was a significant decrease in motor activity below baseline for both the nondominant response letter, $t(51) = 4.67$, $p < .001$, $d = 0.648$ (replication $BF_{10} = 120.70$) and dominant response letter, $t(51) = 3.55$, $p = .001$, $d = 0.491$ (replication $BF_{10} = 44.26$). These results replicate the findings from Experiments 1 and 3 within a single experiment. The findings from Experiment 4 provide further evidence that the suppression of the dominant motor hemisphere observed in a cue-relevant counting task is likely to be a conditioned inhibition effect of preparing for a nondominant hand response, whereas the suppression observed in the response task to new letters is likely an active inhibitory control effect.

DISCUSSION

Here, we showed that abstract cues can be trained to prime the motor system within a single experimental session. This cue-elicited modulation of motor system activity is proposed to be a possible candidate for the neural signature of conditioned action tendencies. Moreover, this form of automatic activity priming was found to be both task dependent and hemisphere specific. Nondominant hemisphere activity did not differ for a cue that previously signaled a dominant versus a nondominant hand response, and this activity was not strongly modulated by current task demands other than selective attention. In contrast, activity in the dominant hemisphere was largely dependent on current task demands. During a cue-relevant counting task, dominant

hemisphere activity was significantly differentiated for a dominant versus nondominant hand cue—increasing for a dominant hand cue and decreasing for a nondominant hand cue. This effect was not observed under identical training and similar testing conditions when the trained response cues were made task irrelevant. Finally, during a cue-irrelevant action selection task, activity in the dominant hemisphere was suppressed to both previously trained cues.

The lack of cue-specific activity in the nondominant hemisphere across the three different task demands was unexpected, particularly so for the cue-relevant counting task (Experiment 1). One predicted pattern of activity was that the nondominant hemisphere would show increased CSE to the trained nondominant hand cue and a decrease in CSE to the trained dominant hand cue, mirroring the pattern observed in the dominant hemisphere for Experiment 1. Instead, the activity observed suggests that this part of the motor system is concerned with action-general rather than action-specific conditioned motor preparation. However, action-specific preparation in the nondominant hemisphere has been observed in a different task setting (e.g., Poole et al., 2018; Leocani, Cohen, Wassermann, Ikoma, & Hallett, 2000). Using a choice RT task, it was shown that when a predictive cue preceded a response cue, activity in the nondominant hemisphere increased while activity in the dominant hemisphere decreased to the predictive cue that signaled an imperative nondominant hand response (Poole et al., 2018). A critical difference between our current study and those showing response-specific preparation in the nondominant hemisphere is the requirement to respond to the trained cues. Whereas these previous studies measured CSE to presentations of current response cues, we measured CSE to presentations of former response cues. Together, these results suggest that controlled motor preparation to the target TMS cues is an important factor in determining how motor priming effects are expressed in the nondominant hemisphere. Alternatively, a different possibility is that cue-specific conditioned action tendencies require extended training to manifest in the nondominant compared with the dominant hand.

In contrast, activity in the dominant hemisphere was highly dependent on the current task demands. Experiment 1, using a cue-relevant counting task, found evidence for cue-consistent conditioned modulation in the motor system. Corticospinal activity was significantly different for a cue that previously signaled a dominant versus nondominant hand response, showing conditioned excitation to the trained dominant hand cue and conditioned inhibition to the trained nondominant hand cue. A similar motor priming effect produced by associative learning processes has been demonstrated using a combined Pavlovian-to-instrumental transfer and a go/no-go task (Freeman et al., 2014). The authors showed that, on go trials, there was an increase in CSE for a conditioned

stimulus that signaled the availability of an appetitive reward. However, no study to date has shown that CSE can be modulated by previously trained response cues presented without any response requirement in the current task. Our results show that motor activity can be conditioned—independently of motivational salience—through associative pairing of a visual cue and a motor response, which subsequently modulates motor system activity through presentations of the cue alone.

Finding evidence for conditioned motor activity provides a candidate mechanism for explaining existing behavioral priming effects in the literature, such as the motor affordance effect. For example, it has been shown that RTs of judgments about the orientation of graspable objects are faster when the handle of the object was directionally congruent with the responding hand (Tucker & Ellis, 1998; see also, Gibson, 1979). Such RT advantages arising from stimulus–response compatibility can be attributed to a lifetime of associating the stimuli (e.g., graspable objects) with motor-congruent actions. A corollary of this extended associative history is that presentations of manipulable objects should elicit congruent motor activation. Indeed, previous research has found that MEPs in the right hand were larger when the handle of a graspable object was oriented toward that hand and that the effect was absent when viewing objects with a broken handle (Buccino, Sato, Cattaneo, Rodà, & Riggio, 2009).

Experiment 2, using a cue-irrelevant counting task, found little evidence for any motor priming effects. This result is surprising given that previous research has shown that graspable objects can activate the motor system even when attention is impaired (McNair et al., 2017; see also Eimer & Schlaghecken, 1998). Similarly, compatibility effects have also been observed when graspable objects are briefly masked (Pappas & Mack, 2008; Tucker & Ellis, 2004; see also Makris, Hadar, & Yarrow, 2013). It is possible that variations in motor priming effects to unattended stimuli across studies reflect differences in training history. Graspable objects, such as tools, have extensive motor action training and should more readily elicit conditioned motor activation outside the focus of attention compared with abstract cues trained within an experimental session. However, no study has yet directly tested the effect of training history on CSE during an inattention task, such as a cue-irrelevant counting task or an attentional blink task (Raymond, Shapiro, & Arnell, 1992).

Experiment 3, using a cue-irrelevant response selection task, found evidence for general motor inhibition. Whereas Experiment 1 provides evidence for cue-specific inhibition in the dominant hemisphere—i.e., a honing of cue-relevant responses—we argue that the inhibition observed in Experiment 3 is due to top–down cognitive control. Rather than being elicited automatically to presentations of a former response cue, goal-directed behavioral control was exerted to prevent action errors to the

no-longer-relevant response cues. This finding is consistent with neurophysiological evidence that response suppression is one method for implementing control over motor activity conditioned through associative learning (Freeman et al., 2014). Interestingly, these results suggest that preparing the motor system for action selection toward replacement cues can help reduce the automatic activation of motor priming effects by formerly trained cues. Therefore, engaging in various forms of alternative behaviors may be an effective strategy for improving impulse control over unwanted actions (e.g., consuming junk food or drug seeking).

Experiment 4, measuring MEPs only from the dominant hand, replicated the findings from Experiments 1 and 3 within the same experiment. The cue-consistent differential priming effect from Experiment 1 and the general motor inhibition effect from Experiment 3 were stable across samples. However, increases and decreases in motor activity from baseline elicited by the dominant versus nondominant response letter during a cue-relevant counting task were statistically significant only when pooling the data across Experiments 1 and 4. The significant main effect of task confirmed that the pattern of motor system activity differs under different task demands. Moreover, the findings suggest that different motor inhibitory processes may be involved between passive-attentional tasks and action selection tasks. For example, when responses are no longer required but the predictive cues are still attended, inhibition of the dominant hemisphere appears to be elicited automatically by a response cue based solely on the prior need to perform a nondominant hand response. In contrast, when responses are still required but to new cues, general inhibition of the dominant motor hemisphere in the presence of either trained cues is activated by top–down suppression based on the current goals to facilitate motor and cognitive control.

Finally, the motor priming effects reported here emerged following a cue–response training session that lasted only 40 min while participants were instructed to withhold responding to the previously trained response cues embedded within a different task. Arguably, these effects underestimate the magnitude of any cue-elicited modulatory effects on the motor system engaged by real-world or well-trained environmental cues, which should have priming effects established over many more learning episodes than were experienced here. Taken together, our results show that motor activity can be conditioned through associative cue–response learning and suggest that well-trained response cues may come to elicit conditioned action tendencies, providing a mechanism for explaining existing behavioral priming effects in the literature. Furthermore, our findings reveal the automatic cognitive and motor processes that are elicited while engaged in a variety of new task demands. These results offer insights into how motor priming may lead to behavioral errors through conditioned motor activation, provide

implications for models of cognitive control, and inform potential strategies for effective behavioral control.

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Notes

1. Supplementary material for this paper can be retrieved from <http://hdl.handle.net/2123/20433>.
2. Note that only 22 participants had complete data from both the Experiment 4 test tasks.
3. Bayesian analysis of the data from Experiment 4, taking the previous experimental data as the prior.

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