Top-down contextual requirement to suppress self-movement influences grasp-specific modulation of corticospinal excitability during action observation

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ABSTRACT

Action observation modulates corticospinal excitability (CSE) measured via TMS in humans, which presumably exposes the effect of mirror neuron activation on corticospinal pathways. These responses can consist of both facilitation and suppression, and the balance of these two may restrict the outflow of activity into movement. Evidence also suggests that task context can considerably influence CSE changes during action observation.

Here, we assessed whether embedding action observation within a Go-NoGo paradigm, which emphasizes movement withholding on observation and NoGo trials, influenced CSE modulation. Fourteen healthy subjects received single pulse TMS over left primary motor cortex (M1) during a baseline period, grasp observation onset, or after a NoGo cue, while performing, observing, or withholding two distinct reach-to-grasp actions. We assessed modulation of MEPs in three intrinsic hand muscles, which were recruited in a grasp-specific manner during action execution.

Although CSE during the task generally increased relative to a pre-task baseline, modulation of grasp observation MEPs relative to an intra-task baseline was limited, and predominantly suppressive in nature both during grasp and NoGo. Seven subjects performed the same task without the NoGo condition ("Go only" block) immediately before the "Go & NoGo" block. Although this still failed to produce overall facilitation, we found evidence for grasp-specific modulation of CSE, which matched the recruitment pattern of the muscles during action execution. Within these subjects, modulation was attenuated when the NoGo condition was introduced, but was still distinct from modulation in the first group.

These results suggest that bottom-up grasp-specific modulation of MEPs during action observation is attenuated by the top-down contextual requirement to suppress self-movement, and facilitation and suppression effects may be determined by the balance between these two processes.

INTRODUCTION

The observation of another's actions induces activity within motor pathways, even in the absence of self-movement. This activity is driven by mirror neurons, which modulate their firing rate during both execution and observation. Mirror neurons were first identified in the macaque ventral premotor area F5[1], and have since been shown to exist in a range of frontal and parietal areas[2–5]. These neurons have been hypothesized to mediate a mapping of observed actions directly onto the motor system of the observer. Mirror activity even extends to pyramidal tract neurons[3,6], which project directly to the spinal cord, and in humans, transcranial magnetic stimulation has demonstrated modulation of corticospinal excitability (CSE) during action observation[7–9]. Importantly, these findings provide evidence for both facilitation and suppression of activity in corticospinal pathways during action observation, and the balance of the two could be critical for preventing the outflow of cortical mirror activity into overt movement[3,10].

A number of TMS studies have shown that the direction and magnitude of CSE modulation during the grasping phase of action observation depends on parameters, such as the force[11] and kinematics[8,12] of observed object-oriented actions. Furthermore, CSE modulation is affected by task instructions or requirements [13,14], as well as the availability and quality of contextual visual information, either regarding the object to be grasped [15,16], or the acting agent [17,18].

One contextual requirement, present in almost all action observation studies, is the requirement to suppress self-movement while observing actions. In TMS studies, subjects are generally required to be at rest since voluntary EMG activity inflates MEP amplitudes. Similarly, since macaque mirror neurons respond to both execution and observation, voluntary EMG during action observation would confound accurate identification of mirror neurons[6]. On the other hand, there has been some speculation that this somewhat artificial requirement to stay relaxed, at least in human studies, may mask or otherwise influence CSE changes during action observation[13,19], and that, importantly, the level of instruction or emphasis on this requirement may contribute to some of the discrepancies in results between studies in terms of facilitation or suppression of CSE.

In this study, we investigated whether the requirement to actively suppress one's own actions influenced CSE modulation during action observation. This requirement was both explicit, via task instructions, and implicit, via embedding the task within a Go-NoGo (execution-observation-NoGo) paradigm, and the fact that observed grasps took place within peri-personal space, which appear to be treated differently within the mirror neuron system [20,21]. Since we hypothesized that the emphasis of the Go-NoGo task in particular on suppression of self-movement might influence CSE modulation during action observation, one group of subjects performed only the Go-NoGo task, while a second group first performed a "Go-only" task involving only execution and observation, and then performed the Go-NoGo task. We hypothesized that grasp-specific modulation during the "Go-only" task might be attenuated by the addition of the NoGo condition due to a shift in the task context.

MATERIALS & METHODS

Participants

14 right-handed subjects (21-41 years old, 8 female) participated in this study. All subjects passed a screening test for contraindications to TMS neurologically healthy, with normal or corrected-to-normal vision. Subjects gave informed consent and were financially compensated for their participation. Experimental procedures were approved by the UCL Local Ethics Committee.

Experimental set-up

Subjects sat opposite an experimenter, rested their hands on two homepads, and viewed two objects through a controllable LCD screen (14x10cm), which remained opaque in between trials (Fig 1a). A marble object afforded PG via opposition of thumb and forefinger, and the sphere object afforded WHG with all fingers encompassing the object (Fig 1a, inset).

Trials began when the subject depressed both homepads and the experimenter depressed the homepad on their side. The LCD screen became transparent (LCDon, Fig 1b.), and the object area was illuminated. After a variable delay (uniformly sampled from 0.25-0.45s), two amber LEDs illuminated on one or other side to indicate the target object for the upcoming trial. After a further variable delay (uniformly sampled from 0.8-1.2s), a single green or red LED indicated the trial type. A green LED on the subject side indicated an execution trial. The subject released their right homepad, and used their right hand to make a reach-to-grasp movement towards the target object. After grasping the object using the required grasp, they rotated the object into a window (> 30degrees), and held the grasp for 1 second. A constant frequency tone indicated that the subject had entered the hold window, and a second, higher frequency tone signaled successful completion of the 1 second hold. The subject then released the grasp, and returned their right hand to the homepad. A green LED on the experimenter side, indicating an observation trial, required the subject to remain still, and simply attend as the experimenter performed the same reach-to-grasp action with their right hand. A red LED indicated a NoGo trial, in which the subject simply refrained from movement. After 1 second, a tone indicated successful completion of the NoGo

trial. A short inter-trial interval (1-2s) occurred between each trial, and all trial types were presented in a pseudo-randomised order. Execution trials were relatively infrequent to reduce the length of the session, but were still included to assess muscle recruitment during action execution, and to encourage subjects to remained attentive throughout the task in case they were required to move.

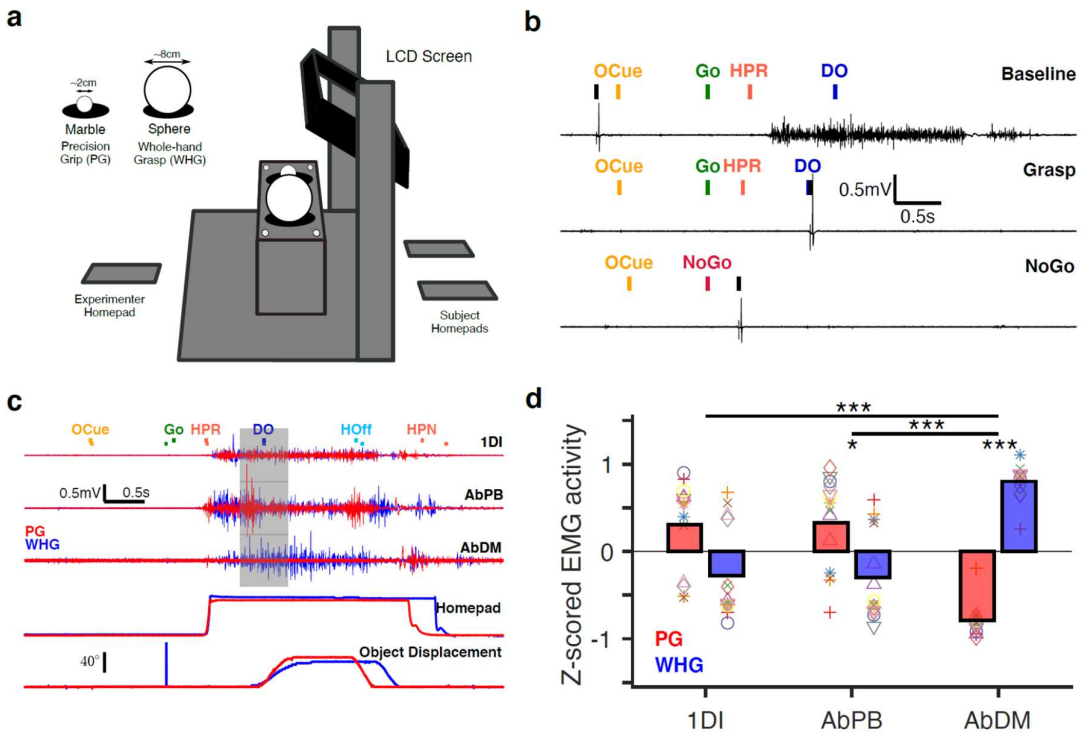

Figure 1. (a) Schematic of experimental box used for task (not to scale). Inset shows marble and sphere objects used for PG and WHG, respectively. **(b)** Example raw EMG activity in 1DI muscle during one precision grip trial of each TMS condition from a single subject. **(c)** Raw EMG activity in each muscle, and homepad and object displacement signals during a single trial of each grasp (red – PG, blue – WHG). Vertical pulse at Go cue on sphere object displacement channel corresponds to TTL pulse used for alignment of digital and analog events. Vertical tick marks denote event times for PG (first row) and WHG (bottom row). Grey shaded area denotes interval (±300ms around DO) used for average EMG shown in (d). **(d)** Z-scored EMG activity for different grasps and muscles, all 14 subjects. Bars show mean, individual subjects shown by symbols. * $p < 0.05$, *** $p < 0.0001$.

Experimental procedure

Single-pulse TMS was delivered on individual trials at one of three possible time points (1) LCDon (Baseline), on either execution or observation trials, (2) Experimenter DO (Grasp) on observation trials (3) 350ms after the red LED on NoGo trials (Fig 1b). On 20% of trials, no TMS was delivered, and all trial types were interleaved in a pseudo-random manner. To maintain attention, subjects completed the experiment in two shorter blocks, with approximately 10 MEPs per condition per block. To assess

whether the presence of the NoGo condition may have influenced the implicit goal of the task and therefore also the modulation of CSE, 7 subjects completed an additional two blocks of the same task, which did not include a NoGo condition, but was identical in all other aspects. These “Go-only” blocks were always completed before the Go & NoGo blocks, and subjects were not introduced to the NoGo condition until these first blocks were completed, in order to keep them immune from the effect of explicit NoGo trials. Prior to each block, a set of 20–30 baseline MEPs were recorded, with the subjects at rest. Before starting the experiment, subjects were briefly familiarized with the task via a short practice session.

TMS and recording

Single-pulse TMS was delivered via a Magstim 200 stimulator attached to a standard figure-of-eight coil (70mm diameter). The coil was held tangentially to the scalp with the handle pointing backwards at a 45°angle to the midline, and the motor hotspot was identified as the position over left M1 eliciting the most consistent MEPs in the three muscles. Stimulator output was set to obtain MEPs averaging approximately 1mV in the resting 1DI muscle.

Electromyographic (EMG) recordings were made from 3 right hand muscles (first dorsal interosseous (1DI), abductor pollicis brevis (AbPB), and abductor digiti minimi (AbDM), using surface electrodes mounted in a belly-tendon montage, with a ground electrode fixed to the bony prominence of the wrist. EMG signals were amplified (x1000), high-pass filtered (3Hz) (Neurolog EMG amplifier NL824, and Neurolog isolator NL820, Digitimer Ltd, UK), and digitised at 5kHz. Concurrently, we recorded the timing of all task events and TMS triggers, and analog signals of homepad pressure and object displacement (5kHz). All data were stored on a laboratory computer for offline analysis.

To quantify the extent to which subjects used each of the three muscles to perform the two grasps, EMG signals were high-pass filtered (0.5Hz, 2nd order Butterworth), rectified, and low-pass filtered (30Hz, 2nd order Butterworth). EMG activity in the -300 to +300ms period around DO was then averaged to obtain a single value for each execution trial. This interval was chosen to capture the dynamic period in which hand

shaping and grasp occurred. For comparison across subjects with different levels of EMG, values within each muscle were z-scored, and averaged for each object. The resulting values were statistically compared via 2-way repeated-measures ANOVA (rmANOVA), with within-subject factors of object (PG, WHG) and muscle (1DI, AbPB, AbDM), followed by post-hoc tests.

Statistical analysis of MEPs

For each subject independently, MEPs were discarded from analysis if; 1) the mean rectified EMG activity in the 100ms preceding the TMS stimulus exceeded 2 standard deviations of the mean pre-stimulus EMG, 2) the peak-to-peak MEP amplitude exceeded 3 standard deviations of the mean MEP amplitude across all conditions in a given block, 3) the MEP amplitude did not exceed 0.05mV. Across all subjects, 5.8±0.3% of MEPs (mean±SEM) were discarded in the “Go & NoGo” block, and 5.0±0.4% of MEPs in the “Go only” block. The peak-to-peak amplitude of remaining MEPs for each subject were averaged across all trials for each condition, to obtain one value per TMS condition, grasp, and muscle for each subject. For comparison to pre-task baseline (Figure 2), these raw MEP amplitudes were used. For all other analyses, MEPs were normalised to the average LCDon baseline across grasps.

To compare MEPs in the pre-baseline period to those during the LCDon baseline and grasping observation, we used a two-way repeated-measures ANOVA (rmANOVA) with factors MUSCLE (1DI, AbPB, AbDM) and CONDITION (Pre-task baseline, LCDon baseline, Grasp), for PG and WHG separately.

MEP modulation within each experimental task was assessed via three-way rmANOVA (factors CONDITION (Baseline, Grasp, NoGo, or Baseline and Grasp) x GRASP (PG,WHG) x MUSCLE (1DI, AbPB, AbDM)). For both experiments, we also compared MEP ratios (PG : WHG) via two-way rmANOVA (CONDITION x MUSCLE). To obtain MEP ratios, PG MEPs for each condition were divided by the corresponding average WHG MEPs. A resulting ratio >1 for a given condition therefore indicated relative facilitation of PG compared to WHG, ratios of <1 indicated relative facilitation of WHG compared to PG, and a ratio of 1 indicated no difference between the objects.

Lastly, we compared the Grasp and NoGo conditions across the two subject groups in the Go & NoGo block, for each object and muscle separately, via 2-way rmANOVA with a within-subject factor of TMS condition (Grasp, NoGo), and between-subject factor of group (1 or 2).

Post-hoc comparisons were conducted where deemed appropriate, and corrected for multiple comparisons (Tukey's honestly significant difference). P-values < 0.05 were considered significant. In cases of non-sphericity for rmANOVAs, Greenhouse-Geisser corrected p-values were used.

RESULTS

In this study, we investigated how CSE modulation during action observation is affected by explicit and implicit task requirements to refrain from self-movement. Subjects observed grasping actions embedded within a Go-NoGo paradigm, which required them to suppress their own movement on most trials. One group of subjects also observed grasping actions in a block without any NoGo condition, prior to completing the Go-NoGo paradigm.

Grasp-specific EMG activity during action execution

During action execution, PG elicited greater activity in 1DI and AbPB muscles, whereas WHG elicited greater activity in AbDM (Fig 1d), as shown by an object x muscle interaction, $F(2,26) = 31.3$, $p = 1.46 \times 10^{-7}$, and post-hoc comparisons of the two objects within each muscle (1DI: $p = 0.057$, AbPB: $p = 0.039$, AbDM: $p = 1.28 \times 10^{-9}$). Pairwise comparisons within object showed that 1DI and AbPB EMG activity was not different ($p = 0.99$), but both muscles had significantly greater PG activity than AbDM, and significantly lower WHG activity (all $p < 0.0001$).

Non-specific facilitation relative to pre-task baseline

We first compared the amplitude of MEPs evoked during the pre-task baseline to those evoked in the LCDon baseline and grasp conditions during the observation task,

across all 14 subjects. For both objects, this revealed a significant main effect of condition (PG: $F(2,26) = 19.15$, $p < 0.0001$, WHG: $F(2,26) = 15.87$, $p < 0.0001$). The main effect of muscle and interaction effects were not significant for either object (all $p > 0.05$). MEP amplitudes were significantly smaller during the pre-task baseline (Fig. 2) compared to both the LCDon baseline (PG: $p = 0.00038$, WHG: $p = 0.00056$), and the grasp period (PG: $p = 0.0019$, WHG: $p = 0.016$). In addition, there was a weak suppression during grasp relative to LCDon baseline (PG: $p = 0.052$, WHG: $p = 0.047$). Given that comparison to the pre-task baseline demonstrated this non-muscle or grasp-specific increase in excitability, we used the LCDon baseline for all subsequent analyses, so that changes relative to this baseline could be more readily attributed to the observation of action (see Discussion).

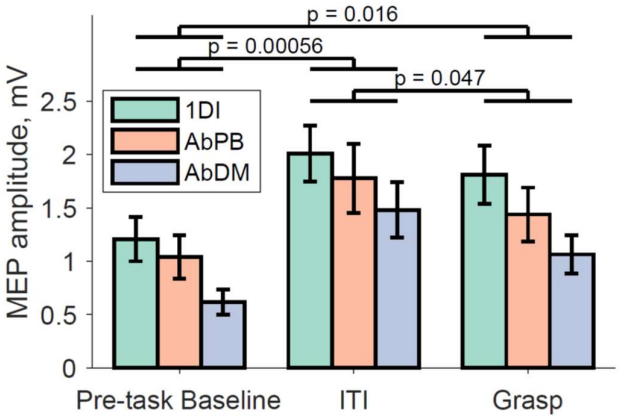

Figure 2. Average raw MEP amplitude across all 14 subjects for pre-task baseline, LCDon baseline, and Grasp (precision grip), for each muscle. Bars show mean±SEM.

Grasp-specific modulation of MEPs in absence of NoGo

To assess the modulation of MEPs during the different task conditions, we compared MEPs during the Go & NoGo task (Fig. 3a-c) across TMS conditions, objects, and muscles via 3-way rmANOVA. Here, we found no significant effects (all main effects and interactions $p > 0.09$). A 2-way rmANOVA (condition x muscle) on the ratio of PG:WHG MEPs (Fig. 3d) also revealed no significant effects (all main effects and interactions $p > 0.16$).

We hypothesized that the presence of the NoGo condition may have shifted the emphasis, or context of the task to suppression of one's own actions (see Discussion), thus diminishing grasp observation-related MEP facilitation, or even producing weak

suppression relative to LCDon baseline, (see Fig. 2). In seven subjects, we therefore assessed corticospinal excitability changes during a block without the NoGo condition, which was always performed before the NoGo block.

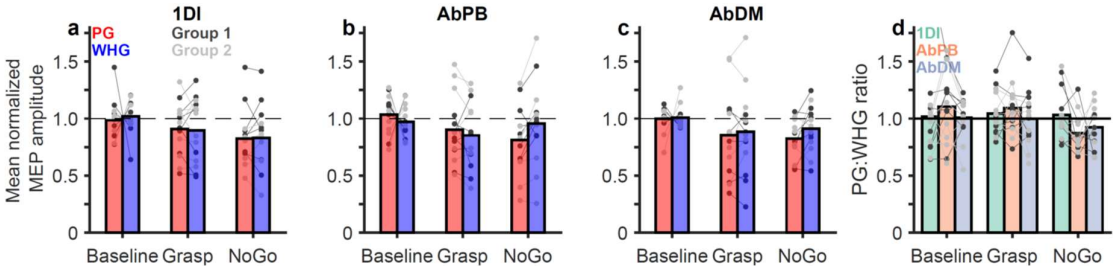

Figure 3. " Go & NoGo" block (n=14). **a-c.** Average normalized MEP amplitude for Baseline and Grasp conditions for each object and muscle. **d.** Ratio of precision grip : whole-hand grasp MEPs. Bars show mean, individual subjects shown by grey lines (dark grey: Group 1, light grey: Group 2).

In this "Go-only" experiment (Fig. 4a-c), there was a 3-way interaction between TMS condition, object, and muscle ($F(2,12) = 4.53$, $p = 0.034$), and a significant TMS condition x muscle interaction in the MEP ratio analysis (Fig. 4d, $F(2,12) = 4.74$, $p = 0.030$). Ratios showed no significant difference between muscles in the Baseline condition (all pairwise comparisons $p > 0.9$). During grasp, 1DI and AbPB ratios were not different ($p = 0.31$), but both were significant larger (PG > WHG) than AbDM ($p = 0.0090$ and $p = 0.00089$ respectively).

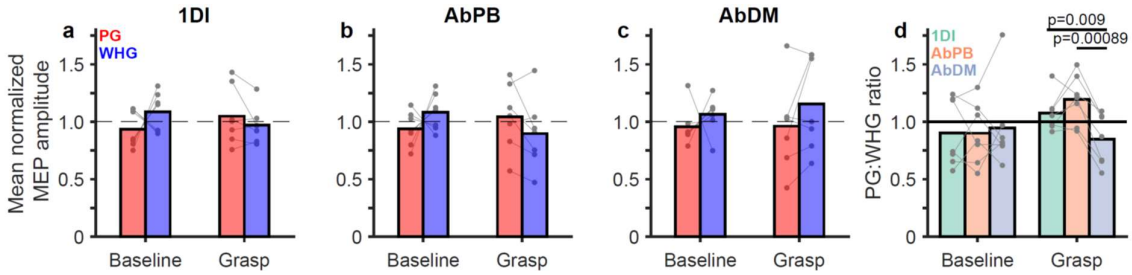

Figure 4. "Go only" block (n=7). **a-c.** Average normalized MEP amplitude for Baseline and Grasp conditions for each object and muscle. **d.** Ratio of precision grip : whole-hand grasp MEPs. All colour conventions as in Figure 3. Bars show mean, individual subjects shown by grey lines.

Finally, we compared MEPs in the Grasp and NoGo condition in the Go & NoGo block across the two groups of subjects (Fig. 5) – those who performed only the Go & NoGo block (Group 1), and those who performed the "Go only" block beforehand (Group 2). In the 1DI muscle, preferentially active during execution of PG, there was a significant TMS condition x group interaction for PG ($F(1,12) = 5.10$, $p = 0.043$), but not for WHG ($F(1,12) = 1.48$, $p = 0.25$). PG grasp MEPs were >20% greater than NoGo MEPs in

Group 2 (p = 0.023), but were not different in Group 1 (p = 0.57). By contrast, the AbDM muscle, preferentially active during execution of WHG, showed a significant TMS condition x group interaction for WHG (F(1,12) = 6.12, p = 0.029), but not PG (F(1,12) = 1.00, p = 0.34). In post-hoc tests, the differences between the Grasp and NoGo condition did not reach significance (Group 1: p = 0.074, Group 2: p = 0.15). In AbPB, interaction effects for both objects were not significant (F(1,12) = 3.48, p = 0.087, WHG: F(1,12) = 2.81, p = 0.12).

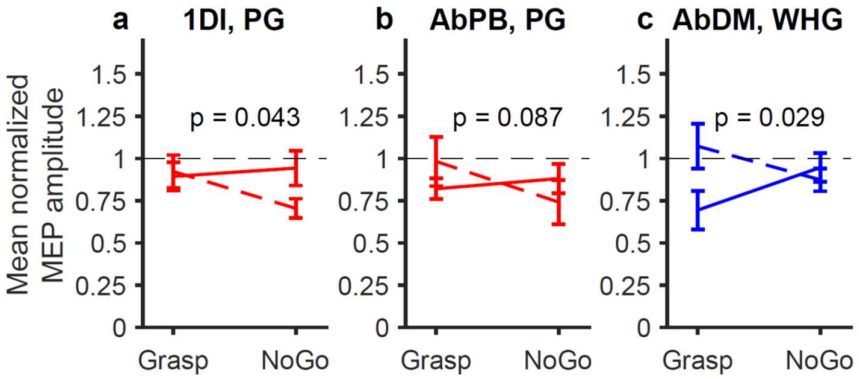

Figure 5. Grasp and NoGo condition normalized MEPs during "Go & NoGo" block for each group of subjects (solid lines: group 1, dashed lines: group 2). For each muscle, MEPs are shown for the grasp which produced greater activation during action execution (precision grip for 1DI and AbPB muscles, whole-hand grasp for AbDM). Data presented as mean±SEM.

DISCUSSION

In this experiment, we aimed to assess the extent to which corticospinal excitability during the observation of naturalistic grasping actions is modulated by the requirement to suppress one's own actions. Specifically, when action observation was embedded within a Go-NoGo paradigm, we hypothesized that grasp-specific modulation during action observation might be attenuated or abolished, since the emphasis of the task increasingly shifted towards global suppression of self-movement.

Action execution recruits muscles in a grasp-specific manner

An important consideration when ascribing modulation during action observation to the mirror neuron system is that execution of the same actions produces muscle-specific activity, which shows some degree of congruence with changes during action observation [7,9]. This was a key aspect of the study by Fadiga and colleagues[7], which reported facilitation of MEPs in three of four muscles (1DI and two arm muscles, but not the opponens pollicis) during observation of arm movements, and recruitment of these same three muscles during action execution.
Despite this, a number of studies using TMS to probe CSE during the observation of naturalistic actions do not always include an 'action execution' condition [9]. The complex activation patterns of hand and arm muscles during different reach to grasp actions [22,23], mean that, for example, it should not be assumed that AbDM is more involved in WHG than thumb and index finger muscles [9]

In the grasping task used in the present study, PG and WHG execution reliably produce different levels of activation in the muscles we recorded (Fig. 1c,d). The 1DI and AbPB muscles showed greater activity during PG, which is consistent with their role in opposition of thumb and forefinger, whereas AbDM, a little finger abductor, showed much higher activity during WHG. This is in line with previous comparisons of EMG activity during PG and WHG performance, as well as in the excitability of PMv-M1 interactions and cortico-cortical inputs to M1 during preparation of different grasps[24].

Non-specific increase in CSE relative to pre-task baseline

In our task, 'baseline' CSE was probed while subjects were at rest in between task blocks, and also at the beginning of some trials, when subjects were still at rest and not observing any grasping action, but engaged in the task.
Our finding of a general (up to twofold) increase in CSE during the task compared to the pre-task baseline (Fig. 2) is quantitatively consistent with other recent results, which have shown significant increases in task MEP amplitude relative to a pre-task baseline, and much smaller changes relative to an intra-task baseline [17,19].

This non-specific increase may have been a consequence of increased attention or arousal during the task period. Although the relationship between gaze and the activity of mirror neurons is variable[25], gaze is often used as a proxy for determining where subject attention is directed. A recent study by Wright et al. found that direction of gaze towards the target object during observation was a significant predictor of increased MEP amplitude[26]. Similarly, D'Innocenzo and colleagues reported that fixation of gaze on a point where maximal detection of biological motion would occur produced increased MEP amplitudes relative to a free gaze condition[27]. Appropriate baseline selection is essential for determining the direction of CSE modulation during action observation, and may partly explain some of the conflicting reports of facilitation or suppression during action observation[9]. In light of the above, and because it is more closely related to the baseline typically used in assessment of mirror neuron firing rates [3], we considered the LCDon baseline a more appropriate choice for quantifying the direction of CSE modulation during grasp observation.

Grasp-specific modulation of CSE

When subjects merely executed or observed grasping actions, we found a grasp-specific modulation of excitability during observation of PG and WHG (Fig. 4), which was not apparent when the task was completed with a NoGo condition (Fig. 3). MEPs were larger in PG compared to WHG in the 1DI and AbPB muscles, but smaller in AbDM, consistent with several TMS studies which have demonstrated muscle or grasp-specific changes in excitability during action observation [7,17,28,29]. The study by Bunday et al. found greater excitability in the 1DI muscle during observation of videos of PG compared to WHG. Notably, this modulation largely occurred while MEPs were

suppressed relative to the inter-trial interval baseline. Additionally, this interaction, when controlling for the size of the observed hand, was present when viewing the hand only, but not a whole-person actor [17]. In our study, although the whole actor was visible to the subject, the LCD screen effectively ensured that the subject's field of view around the objects when looking through the screen was limited to include only the forearm and hand of the experimenter. Our study also differed in the fact that actions were performed by a live actor, rather than viewed on video, occurred in operational and metric peri-personal space, and from a frontal, rather than side viewpoint. In macaque mirror neurons, live actions tend to produce greater activation than video-ed ones [30], and some mirror neurons fire in a space- [20,21] and view-point [30] dependent manner. Although these distinctions render detailed comparisons challenging, we did find a similar grasp-specific modulation in intrinsic hand muscles during observation of PG and WHG, suggesting that under certain conditions, observation of action induces muscle-specific changes in CSE. These changes also parallel the recruitment of muscles during performance of those same actions (Fig. 1c,d), indicating that CSE modulation during action observation reflects activation of the human mirror neuron system.

Task context modulates CSE

In our study, we found that the presence of the NoGo condition, which required subjects to refrain from self-movement in the same way as during observation trials, attenuated grasp-specific modulation during action observation (Figs. 3 & 4). On the other hand, differences between the two groups of subjects in the NoGo block (Fig. 5), suggest that the Go-only block influenced MEP modulation in the subsequent Go & NoGo block, such that suppression was largely limited to the NoGo condition, rather than spanning across both Grasp and NoGo conditions. Taken together, these results suggest that the context or emphasis of the task on observation of action versus suppression of self-movement work in opposite directions, and may contribute to the balance of facilitation and suppression seen in CSE during the action observation task.

On the face of it, the rapid, automatic onset of activity in mirror neurons during action observation in a circuitry extending from parietal to frontal areas implies that bottom-

up visual input is the predominant driver of mirror neuron activity. However, there is a wealth of evidence that context cues play an equally, if not more, important role. In macaque mirror neurons with ventral premotor cortex, knowledge of a grasping action taking place, even if is not visible to the observing monkey, is sufficient to elicit activity in many mirror neurons [31]. Similarly, modulation of CSE in humans can persist even in the absence of direct visual input [13,32]. On the other hand, unexpected kinematics can abolish CSE changes during action observation [8], and although kinematic cues are sufficient for CSE modulation according to weight during observed object lifting [15,33], incongruent cues (e.g. heavy weights labelled as light) also abolish MEP facilitation, and can even induce overall suppression [15]. Alternatively, incongruent weight labels replace the weight-based modulation with a general 'expectation-monitoring' one[16]. This study further showed that virtual lesioning of posterior superior temporal sulcus can restore weight-based modulation, whereas lesion of dorsolateral prefrontal cortex abolished both forms of modulation, supporting the idea that CSE modulation is susceptible to higher-level cognitive influence[16].
Another recent study comparably found that reliable contextual cues were sufficient to elicit muscle-specific CSE changes when visual kinematic cues were absent, and that CSE modulation was strongest when both contextual and kinematic cues were present [18]. In the authors' framework, M1 is the site of convergence for bottom-up kinematic cues regarding the actual observed action, presumably arriving via the parieto-frontal grasping circuitry which houses mirror neurons [34], and top-down contextual cues or priors. These two streams of information may be combined within a Bayesian predictive coding framework [35], enabling the observer to infer, or predict, the outcome or intention of the observed movement [8].

The interactions between movement suppression during action observation and during NoGo in the present task appear to contrast with a previous study of action observation and NoGo responses in macaque mirror neurons[36] where 'execution NoGo'-responding neurons and mirror neurons rarely overlapped. However, these neurons were recorded in ventral premotor area F5, where population-level mirror activity is distinct from that in M1[10]. In addition, information about trial type (execution, observation, NoGo) in the present task, was provided at the equivalent time moment on each trial, whereas the mirror neuron study examined execution and observation responses in separate blocks. In our task, the presence of the two objects in peri-

personal space may also have engendered a closer relationship between action observation and NoGo, as the possibility to interact with the objects increases the relevance of appropriate and timely movement suppression. In line with this, some mirror neurons are known to preferentially encode peri-personal space [20], including in an operational manner, suggesting that the possibility of object interaction is a salient contextual factor contributing to modulation during action observation.

Our results demonstrate that although a grasp-specific 'motor resonance' effect can be elicited by action observation, this effect is not robust, and its magnitude and direction are influenced by the top-down requirement to suppress action. This sits within a growing body of evidence indicating that the overall modulation of CSE during action observation is the net result of the interplay between bottom-up visual input and top-down cognitive contextual cues and priors.

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Figure 1.

(a) Schematic of experimental box used for task (not to scale). Inset shows marble and sphere objects used for PG and WHG, respectively.

(b) Example raw EMG activity in 1DI muscle during one precision grip trial of each TMS condition from a single subject.

(c) Raw EMG activity in each muscle, and homepad and object displacement signals during a single trial of each grasp (red – PG, blue – WHG). Vertical pulse at Go cue on sphere object displacement channel corresponds to TTL pulse used for alignment of digital and analog events. Vertical tick marks denote event times for PG (first row) and WHG (bottom row). Grey shaded area denotes interval (±300ms around DO) used for average EMG shown in (d).

(d) Z-scored EMG activity for different grasps and muscles, all 14 subjects. Bars show mean, individual subjects shown by symbols. * $p < 0.05$, *** $p < 0.0001$.

Figure 2.

Average raw MEP amplitude across all 14 subjects for pre-task baseline, LCDon baseline, and Grasp (precision grip), for each muscle. Bars show mean±SEM.

Figure 3.

"Go & NoGo" block (n=14). **a-c.** Average normalized MEP amplitude for Baseline and Grasp conditions for each object and muscle. **d.** Ratio of precision grip : whole-hand grasp MEPs. Bars show mean, individual subjects shown by grey lines (dark grey: Group 1, light grey: Group 2).

Figure 4.

"Go only" block (n=7). **a-c.** Average normalized MEP amplitude for Baseline and Grasp conditions for each object and muscle. **d.** Ratio of precision grip : whole-hand grasp MEPs. All colour conventions as in Figure 3. Bars show mean, individual subjects shown by grey lines.

Figure 5.

Grasp and NoGo condition normalized MEPs during "Go & NoGo" block for each group of subjects (solid lines: group 1, dashed lines: group 2). For each muscle, MEPs

are shown for the grasp which produced greater activation during action execution (precision grip for 1DI and AbPB muscles, whole-hand grasp for AbDM). Data presented as mean±SEM.