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The intracortical excitability changes underlying the enhancing effects of rewards and punishments on motor performance

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ABSTRACT

Monetary rewards and punishments enhance motor performance and are associated with corticospinal excitability (CSE) increases within the motor cortex (M1) during movement preparation. However, such CSE changes have unclear origins. Based on converging evidence, one possibility is that they stem from increased glutamatergic (GLUTergic) facilitation and/or decreased type A gamma-aminobutyric acid ($GABA_A$)-mediated inhibition within M1. To investigate this, paired-pulse transcranial magnetic stimulation was used over the left M1 to evaluate intracortical facilitation (ICF) and short intracortical inhibition (SICI), indirect assays of GLUTergic activity and $GABA_A$-mediated inhibition, in an index finger muscle during the preparation of sequences initiated by either the right index or little finger. Behaviourally, rewards and punishments enhanced both reaction and movement time. During movement preparation, regardless of rewards or punishments, ICF increased when the index finger initiated sequences, whereas SICI decreased when both the index and little fingers initiated sequences. This finding suggests that GLUTergic activity increases in a finger-*specific* manner whilst $GABA_A$-mediated inhibition decreases in a finger-*unspecific* manner during preparation. In parallel, both rewards and punishments non-specifically increased ICF, but only rewards non-specifically decreased SICI as compared to neutral. This suggests that to enhance performance rewards both increase GLUTergic activity and decrease $GABA_A$-mediated inhibition, whereas punishments selectively increase GLUTergic activity. A control experiment revealed that such changes were not observed post-movement as participants processed reward and punishment feedback, indicating they were selective to movement preparation. Collectively, these results map the intracortical excitability changes in M1 by which incentives enhance motor performance.

1. Introduction

Monetary rewards and punishments are known to enhance motor performance [1,2] by facilitating the processes underlying movement preparation [3–11]. For instance, Freeman and Aron (2014) [6] used transcranial magnetic stimulation (TMS) over the primary motor cortex (M1) to show that rewarded stimuli, as compared to neutral ones, quickened reaction time and increased corticospinal excitability (CSE) during movement preparation. Whilst this indicates that brain activity changes during movement preparation are associated with incentive-induced (reward/punishment) improvements in motor performance, the origins of such CSE changes remain unclear. Namely, changes in CSE reflect the excitability of cortical, subcortical, as well as spinal structures [12], which can further reflect an increase in glutamatergic (GLUTergic) and/or a decrease in gamma-aminobutyric acid (GABA)ergic activity [13,14]. Importantly, rewards and punishments are increasingly recognised as potential enhancers of rehabilitation following physical and brain insults [15–18]. Therefore, elucidating their mechanisms of action could lead to improved therapeutic interventions [19]. This work sought to characterise the intracortical excitability changes occurring within M1 when motor performance is enhanced by rewards and punishments.

Converging lines of evidence suggest that rewards and punishments enhance performance by altering M1's intracortical GLUTergic and type A GABA ($GABA_A$) activity during movement preparation. First, M1 has been shown to significantly contribute to reward and punishment processing [20,21]. Albeit such processing encompasses multiple brain areas [22,23], this evidence suggests that rewards and punishments

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induce circuit-specific changes in M1[20,21]. Second, human anatomical evidence shows that ~67% of M1's neurons are projecting GLUTergic pyramidal neurons whilst ~33% of M1's neurons are local GABA interneurons [24]. Assuming that CSE changes induced by rewards and punishments have some cortical origins, one tentative possibility is that they originate from intracortical GLUTergic neurons and GABA interneurons in M1. To date, no study has evaluated the effects of rewards and punishments on GLUTergic and GABA circuits in M1 during movement preparation. Nonetheless, human TMS studies strongly suggest that movement preparation releases M1's intracortical $GABA_A$-mediated inhibition [25–27], pointing to the role of local GABAergic activity in mediating movement preparation. Whether movement preparation entails changes in M1's GLUTergic activity remains unclear in humans but this proposition is supported by animal work [28,29]. Overall, this evidence suggests that any performance enhancements induced by rewards and punishments entails changes in M1's GLUTergic and $GABA_A$ activity during movement preparation.

Although not focusing on movement preparation, parallel evidence also suggests that incentives alter M1's intracortical GLUTergic and $GABA_A$-mediated activity. Namely, previous work has shown that the ventral tegmental area (VTA) alters M1's excitability [30] through GLUTergic [31] and dopaminergic signalling [32] by activating type 2 dopamine (D2)-like receptors [33] located on $GABA_A$ (parvalbumin-expressing) interneurons [34]. Given the well-established role of VTA neurons in processing both rewards and punishments [35,36], this pathway could underpin changes in GLUTergic activity and $GABA_A$-mediated inhibition in M1 that lead to the invigorating effects of incentives on motor performance. In further support of this, pharmacological work has shown that memantine [37] (an N-methyl-*d*-Aspartate [NMDA] receptor antagonist), diazepam [38] (a $GABA_A$ agonist) and ethyl alcohol [39] (an NMDA antagonist and $GABA_A$ agonist) alter behavioural responses to rewards and punishments. Collectively, this evidence suggests that incentives alter intracortical GLUTergic activity and $GABA_A$-mediated inhibition in M1, but whether these alterations account for the enhancing effects of rewards and punishments on motor performance remains unknown.

In this light, the objective of this work was to investigate if rewards and punishments enhance motor performance by altering intracortical GLUTergic activity and $GABA_A$-mediated inhibition in M1 during movement preparation. To investigate this possibility, neuronavigated paired-pulse TMS (ppTMS) was used over M1 to evaluate intracortical facilitation (ICF) and short intracortical inhibition (SICI), indirect assays of GLUTergic activity and $GABA_A$-mediated inhibition [14,40]. It was hypothesised that rewards and punishments would both increase ICF during preparation [31], suggesting that incentives utilise a common GLUTergic pathway in M1 to enhance motor performance. Although rewards were expected to alter SICI [41–43], whether the SICI decreases expected to occur during movement preparation [25–27] would be altered by incentives could not be hypothesised *a priori*.

2. Methods

2.1. Participants

Two groups of 20 right-handed, medication-free, and self-reported neurologically healthy participants took part in the ICF (23.9 ± 0.7 years old; 9 females) and SICI Experiments (24.5 ± 1.3 years old; 15 females). Participants were screened for TMS contraindications [45] and provided their informed written consent (approved by the local institutional board; project # ERN_17-1541AP6). Participants were not excluded based on whether they showed significant ICF or SICI. Participants were paid a minimum of £20, which was topped up with their performance-based earnings. Overall, participants earned an average of £35.03 ± 0.83. For both the ICF and SICI experiments, the same participants completed both the Movement Preparation and Feedback Processing sessions. All sessions were counterbalanced across participants to mitigate carry-over effects [46] and, for a given participant, took place at the same time of day to control for circadian influences of excitability [47,48]. On average, 5.1 ± 1.8 days and 2.9 ± 0.8 days separated the Movement Preparation and Feedback Processing sessions of the ICF and SICI Experiments, respectively. A total of 80 TMS sessions, each lasting approximately 2h30, were performed in this study.

2.2. Task and timing

The task consisted of executing 4-element finger-press sequences as fast and accurately as possible following the onset of a visual GoCue (Figs. 1A and 3A). To investigate motor performance enhancements, participants executed the 4-element finger-press sequences under Reward (Max: +£0.6; Min: +£0.0), Neutral (Max: +£0.0; Min: +£0.0), and Punishment conditions (Max: +£0.0; Min: £0.6). The magnitude of rewards or punishments obtained was a decay function (Figs. 1B and 7B) of participants' total execution time (defined as the sum of reaction and movement time) on a given trial.

The 4-element finger-press sequences selectively comprised index and little finger presses executed with the right hand, which were set as the "D" and "J" keyboard keys and labelled as digits "1" and "4", respectively. Doing so resulted in 6 possible 4-element finger-press sequences: "1-1-4-4", "1-4-1-4", "1-4-4-1", "4-4-1-1", "4-1-4-1", and "4-1-1-4". The sequences were pseudorandomised into 24-trial cycles, each trial containing a single 4-element finger-press sequence. The trials (sequences) were equiprobable amongst Reward, Neutral, and Punishment conditions (see below). Trials were pseudorandomised such that the same 4-element finger-press sequence or Incentive condition (Reward, Neutral, Punishment) was never repeated on adjacent trials. Moreover, there were an equal number of 4-element finger-press sequences that were initiated with the index ("1") and little ("4") fingers.

Within a 24-trial cycle, the Reward (8 trials), Neutral (8 trials), and Punishment conditions (8 trials) each comprised 3 single pulses to evaluate CSE, 3 paired-pulse trials (either ICF or SICI), and 2 NoTMS trials. Each of the 3 single- and paired-pulse trials was delivered at one of the 3 different time points (Figs. 1 and 7, see below for a justification of the chosen time points). Each session consisted of a total of 432 trials (324 TMS and 108 NoTMS trials), which were separated into three Blocks of 144 trials (108 TMS and 36 NoTMS trials) each lasting ~25min. Short breaks were provided to participants every 48 trials, to prevent the accumulation of fatigue.

2.3. Typical trial chronology

For both sessions of each Experiment (Figs. 1A and 7A), a trial was initiated by displaying the Incentive Cue ("Reward +£0.6", "Neutral +£0.0", or "Punishment -£0.6") for 1,500 ms. To make the cues more salient, green-, grey-, and red-coloured fonts were used for the Reward, Neutral, and Punishment Incentive Cues, respectively. The GoCue was then displayed and consisted of the 4-element finger-press sequence to be executed. Participants were allowed a total of 1,750 ms to execute the sequence ("Allowed Execution Time" in Figs. 1A and 3A). Once the 4 keys were pressed or the 1,750 ms limit was reached, whichever came first, the screen went black for a delay of 1,000 ms. The Incentive Feedback was then displayed for 2,000 ms, followed by the Execution Time of the ongoing trial for 1,500 ms. Then, the trial ended with a black screen. A fixed inter-trial interval of 1,500 ms separated each trial. Each trial lasted ~8,500 ms, allowing sufficient time for the TMS stimulators to recharge between each trial.

2.4. Apparatus

All 4-element finger-press sequences were executed on a USB-wired keyboard (600 Microsoft ®). All visual stimuli were displayed on a 24-inch iiyama Prolite (B2409HDS) computer monitor (1920 × 1080 pixels; vertical refresh rate [55–75 Hz]). The behavioural experiments

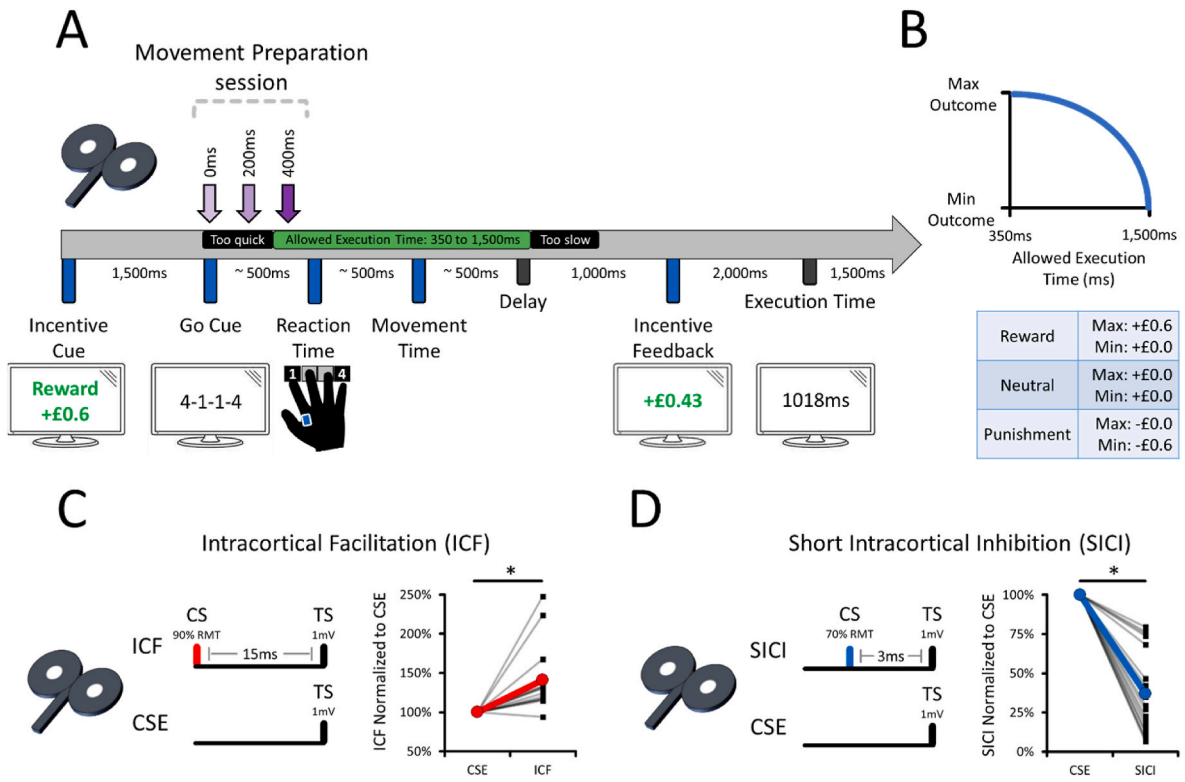

Fig. 1. Assessment of ICF and SICI during the Movement Preparation session. (A) *Chronology of a typical trial.* For both ICF and SICI, TMS was delivered either at GoCue onset (i.e., 0 ms), 200 ms or 400 ms later. The TMS data were later pooled according to the percentage of the reaction time (RT) at which pulses were delivered (<50% for the Early RT and >50% for Late RT). Although participants executed the sequences by using their right index and little fingers, TMS-evoked responses were recorded from the right FDI muscle only (depicted as a blue electrode). This was to determine if TMS-evoked responses were selectively present when initiating sequences with the right index or little finger, which would inform about the degree of finger-*specificity* of the excitability changes. **(B)** *The decay function used to adjust the incentives based on performance.* "Max" and "Min" refer to the maximal and minimal possible outcome on a given trial. Allowed execution time is defined as the sum of RT and movement time (MT; as depicted in panel A). **(C)** *The TMS parameters for the ICF Experiment (n = 20)* successfully induced ICF at rest, as assessed by delivering 30 single pulses and 30 paired ICF pulses. **(D)** *The TMS parameters for the SICI Experiment (n = 20)* successfully induced SICI at rest, as assessed by delivering 30 single pulses and 30 paired SICI pulses. For panels (C) and (D), individuals' data with their respective means are shown [44]. RMT means resting motor threshold. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

were run through custom-built scripts using MatLab (R2021b; MathWorks ®) and the PsychToolBox-3 interface. To calculate finger press timing, the PsychToolBox-3 function "KbQueueCheck" was used, resulting in submillisecond (>1,000 Hz) sampling of finger presses.

A USB-wired Arduino Nano board with a Deek Robot Terminal Adapter was controlled through MatLab to externally trigger the TMS stimulators by sending rising edge 5 V triggers. Based on 800 behavioural trials and bootstrapped estimations (100,000 samples), the Arduino hardware had a latency of ~20 ± 3 ms between issuing the MatLab command and the delivery of a single 5 V trigger. This was offset by sending the 5 V triggers 20 ms earlier than the predefined time points in both the Movement Preparation and Feedback Processing sessions. Moreover, ICF and SICI paired-pulse trials were triggered 15 and 3 ms earlier than the single-pulse (CSE) trials, respectively. This was to account for the inter-pulse intervals on paired-pulse TMS trials (see below), allowing test stimuli to be delivered at a similar latency on single and paired-pulse trials.

2.5. EMG system and neuronavigated TMS

Electromyography (EMG) data from the right FDI muscle belly were recorded through a single bipolar electrode connected to a 2-channel Delsys Bagnoli (Delsys ®) system, itself connected to a Micro 1401 data acquisition unit (Cambridge Electronic Design). The EMG data were acquired with Signal (Cambridge Electronic Design, v6.05) at a sampling rate of 10,000 Hz for epochs of 500 ms (200 ms pre-trigger time). The EMG data were high- and low-pass filtered at 20 Hz and 450 Hz, respectively, with a notch at 50 Hz. The reference EMG electrode was positioned on the proximal olecranon process of the right ulnar bone. The EMG data were analysed using an automated custom-built Matlab script. In this work, only the data from the right FDI were recorded. Namely, the FDI is a co-agonist of the index finger flexions required for button presses [49]. It was reasoned that if FDI activity would increase when the index finger initiated sequences, but not when the little finger did, this would allow exploring if the excitability changes are specific to the finger that initiated sequences. Hereafter, the term "finger-specific" refers to excitability changes observed selectively when the index or little finger initiated sequences. Oppositely, the term "finger-unspecific" refers to excitability changes observed when both the index and little fingers initiated sequences.

Neuronavigated TMS pulses were delivered through a single figure-of-eight 70 mm Alpha Flat Coil (uncoated) connected to a paired-pulse BiStim [2] stimulator (MagStim, Whitland, UK). BrainSight (Rogue Research; Montreal, Canada) was used to ensure reliable coil positioning during every experiment and session [50]. The coil was positioned at a 45° angle in a posterior-anterior axis over the FDI motor hotspot of the left M1, defined as the area where MEPs of maximal amplitude could be reliably elicited with suprathreshold pulses. The resting motor threshold (RMT) was defined as the % of maximum stimulator output to induce 5 out of 10 MEPs of at least 50 μV of peak-to-peak amplitude [51]. For every participant, the FDI motor hotspot, the RMT, and the test stimulus intensity (see below) were assessed at the start of every session. For both sessions of the ICF and SICI Experiments, the average RMTs were 49 ± 2% and 51 ± 2% of the maximum stimulator output, respectively.

For both sessions of the ICF and SICI Experiments, ICF and SICI were *respectively* induced by delivering conditioning pulses at 90% and 70% of the RMT [52]. Inter-pulse intervals of 15 ms and 3 ms were selected to induce ICF and SICI [40], respectively. For both ICF and SICI, test stimulus (TS) intensity was calibrated to induce motor-evoked potentials (MEPs) of ± 1 mV at rest. Alongside ICF and SICI, single pulses of TMS at TS intensity were delivered to evaluate CSE. For both sessions of the ICF and SICI Experiments, the average TS intensities were 58 ± 2% and 62 ± 3%, respectively.

2.6. TMS delivery time points

For the Movement Preparation session (Fig. 1A), TMS pulses were delivered at GoCue onset (0 ms) as well as 200 ms and 400 ms following cue onset to investigate excitability changes in M1. These time points were chosen based on previous TMS work using similar timings to show reward-induced excitability changes during movement preparation [6,8,43]. They were also chosen to provide a measure of excitability during the first (<50%) and second halves (>50%) of the reaction time (RT) period [7,25,53], which was deemed critical to investigate the evolution of excitability during movement preparation.

For the Feedback Processing session (Fig. 7A), TMS pulses were delivered at Feedback (FB) Onset (0 ms) as well as 500 ms and 1,000 ms following FB Onset to investigate excitability changes in M1. These time points were also chosen based on previous TMS work using similar timings to show reward- and punishment-induced excitability changes during feedback processing [41,54].

For the Movement Preparation session only, the TMS data were first pooled according to the percentage of the RT period at which pulses were delivered (Fig. 1A). This was because reaction times were variable, but TMS was delivered at fixed time points, implying that TMS pulses were unlikely to be systematically delivered at a similar latency during the RT period across trials. TMS pulses delivered at a latency below and above 50% of the RT were pooled together and defined as Early RT and Late RT, respectively. Pulses delivered at GoCue onset were not pooled differently, since their delivery precisely coincided with the start of the RT period. Hereafter, the 200 ms and 400 ms time points in the Movement Preparation session are referred to as Early RT and Late RT, respectively. For the Feedback Processing session, TMS data were independent of RT and were thus pooled according to their delivery time points.

2.7. Number of TMS trials per condition

For both the ICF and SICI Experiments, a total of 18 TMS trials were delivered per TMS variable (CSE, ICF or SICI), level of Incentives (Reward, Neutral, Punishment), and Time Points (GoCue, Early RT, Late RT or FB Onset, 500 ms, 1,000 ms). This resulted in a total of 324 TMS trials (out of 432 behavioural trials) per session. After trial rejection (see below), the number of trials exceeded current guidelines to reliably assess excitability changes (TMS without neuronavigation [55]: 30 trials for ICF and 26 for SICI; TMS with neuronavigation [56]: 25 trials for ICF and 20 trials for SICI). See Tables 1 and 2 for a complete report of the average number of trials included in the analyses of the ICF and SICI Experiments. Overall, more than 30 trials were included for the main effects of Incentives and Time Points for each TMS variable (CSE, ICF, and SICI).

2.8. Dependent variables

The behavioural dependent variables were reaction and movement time, as well as Accuracy (success rates). RT was defined as the time difference in milliseconds between GoCue onset and the first finger keypress. Movement time (MT) was defined as the time difference in milliseconds between the first and fourth finger keypress. Accuracy was defined as a binary variable denoting if participants executed the correct sequence within the allowed execution time (Figs. 1A and 3A).

Table 1
ICF experiment.

Movement Preparation session					
CSE Trials					
Main Effect of Incentives			Main Effect of Time Points		
Reward	Neutral	Punish	GoCue	Early RT	Late RT
51.6 ± 0.6	52.3 ± 0.5	51.5 ± 0.7	52.6 ± 0.6	55.0 ± 1.9	38.1 ± 2.0
ICF Trials					
Main Effect of Incentives			Main Effect of Time Points		
Reward	Neutral	Punish	GoCue	Early RT	Late RT
49.7 ± 0.8	49.9 ± 0.7	49.6 ± 0.9	53.1 ± 0.6	61.0 ± 2.9	35.1 ± 2.3
Feedback Processing session					
CSE Trials					
Main Effect of Incentives			Main Effect of Time Points		
Reward	Neutral	Punish	FB Onset	500 ms	1000 ms
52.7 ± 0.7	52.4 ± 0.7	51.8 ± 0.8	52.2 ± 0.8	52.3 ± 0.7	52.3 ± 0.7
ICF Trials					
Main Effect of Incentives			Main Effect of Time Points		
Reward	Neutral	Punish	FB Onset	500 ms	1000 ms
52.7 ± 0.7	52.8 ± 0.6	51.7 ± 0.8	52.4 ± 0.8	52.1 ± 0.7	52.8 ± 0.6

The descriptive statistics represent the mean (±SEM) number of valid TMS trials included in the analyses of the ICF Experiment.

Table 2
SICI experiment.

Movement Preparation session					
CSE Trials					
Main Effect of Incentives			Main Effect of Time Points		
Reward	Neutral	Punish	GoCue	Early RT	Late RT
50.5 ± 0.9	51.6 ± 1.0	50.1 ± 1.0	51.5 ± 0.9	55.1 ± 2.8	35.7 ± 2.1
SICI Trials					
Main Effect of Incentives			Main Effect of Time Points		
Reward	Neutral	Punish	GoCue	Early RT	Late RT
44.1 ± 1.6	44.1 ± 2.0	43.5 ± 2.1	46.8 ± 2.1	47.3 ± 2.8	37.7 ± 2.0
Feedback Processing session					
CSE Trials					
Main Effect of Incentives			Main Effect of Time Points		
Reward	Neutral	Punish	FB Onset	500 ms	1000 ms
53.4 ± 0.4	53.2 ± 0.4	53.5 ± 0.3	52.9 ± 0.4	53.7 ± 0.4	53.4 ± 0.2
SICI Trials					
Main Effect of Incentives			Main Effect of Time Points		
Reward	Neutral	Punish	FB Onset	500 ms	1000 ms
50.7 ± 1.1	50.9 ± 1.2	50.8 ± 1.3	51.6 ± 1.1	50.5 ± 1.2	50.3 ± 1.4

The descriptive statistics represent the mean (±SEM) number of valid TMS trials included in the analyses of the SICI Experiment.

The TMS dependent variables were calculated as MEP peak-to-peak amplitude upon delivery of single (CSE) and paired TMS pulses (ICF or SICI). For single pulses (CSE), MEP peak-to-peak amplitudes were calculated as (non-normalised) values in mV and averaged separately for each level of Incentives, Time Points, session, and Experiment. For paired pulses, MEP peak-to-peak amplitude on ICF and SICI trials were calculated similarly. Then, the individual ICF and SICI trials were

separately normalised as a percentage (%) of their corresponding CSE average. Subsequently, the normalised individual ICF and SICI trials were averaged separately for each level of Incentives, Time Points, session, and Experiment.

2.9. Behavioural and TMS trial rejection

Behavioural trials on which RTs were below 200 ms were rejected from the analyses, as these trials were indicative of premature responses. To prevent the contamination of muscle pre-activation in TMS data, TMS trials where the average root mean square of the FDI EMG amplitude exceeded 100 μV in the 50 ms before the TMS stimulator was triggered were removed from analyses (similar to Ref. [57]). Finally, for the Movement Preparation session only, the TMS pulses at 400 ms that were delivered to a latency >100% of RT were rejected since TMS pulses would then be delivered during movement execution (outside of preparation). For both sessions and Experiments, this resulted in a total rejection of 2.7% of all trials (936 out of 34,560 trials).

2.10. Statistical analyses

The main analyses were conducted using generalised mixed models [58,59], with a gamma distribution to account for the positive continuous skewness of the RT, MT, CSE, ICF, and SICI data [60]. To analyse Accuracy, generalised mixed models with a binomial distribution were conducted because this variable was binary (on a trial-per-trial basis). For each model, the maximally complex random effect structure (random intercepts for Participants and random slopes for all of the Fixed Effects and Interactions, wherever the data allowed their inclusion) that minimised the Akaike Information Criterion (AIC) was chosen to analyse the results [61].

For the Movement Preparation session, the fixed effects to analyse behavioural data were Incentives (Reward, Neutral, Punishment) and TMS Trial Types (NoTMS, CSE, ICF or SICI). The fixed effects to analyse TMS data were Incentives (Reward, Neutral, Punishment), Time Points (GoCue, Early RT, Late RT) and Initiating Finger (Index, Little). For the Feedback Processing session, the fixed effect to analyse behavioural data was Incentives (Reward, Neutral, Punishment). For those models, the effects of TMS Trial Types and Initiating Finger were not included because TMS pulses were delivered >1,000 ms after movement completion [41,54]. The fixed effects to analyse TMS data were Incentives (Reward, Neutral, Punishment) and Time Points (FB Onset, 500 ms, 1000 ms). The fixed effects were the same for the ICF and SICI Experiments.

P values below 0.05 were determined as statistically significant. The Benjamini-Hochberg (1995) [62] correction was used to correct p values for multiple comparisons. To report statistics, the mean ± 1 SEM was used throughout. All analyses were conducted in JAMOVI (version 2.3.16) [63].

2.11. Data availability

This work's data are freely available and can be obtained as an Excel spreadsheet from the following URL: https://osf.io/96u7q/

3. Results – movement preparation

3.1. ICF and SICI were reliably observed at rest

To ensure the chosen TMS parameters reliably induced ICF and SICI (Fig. 1C and D), 30 TMS trials were recorded for CSE, ICF, and SICI at rest before participants executed the finger-press sequences. The results revealed significant M1 facilitation with ICF (Fig. 1C; 1.265 ± 0.155 mV) as compared to CSE (0.912 ± 0.111 mV; $p < 0.0001$). In addition, there was significant M1 inhibition with SICI (Fig. 1D; 0.328 ± 0.074 mV) as compared to CSE (1.051 ± 0.161 mV; $p < 0.0001$). This confirms that ICF and SICI were reliably observed at rest.

3.2. Finger-specific CSE changes during movement preparation

These analyses assessed if Time Points altered CSE during preparation. For the ICF Experiment, the CSE data (Fig. 2A–B) revealed a Time Points * Initiating Finger interaction ($\chi^2 = 20.890$; $p < 0.0001$). The interaction revealed a simple effect of Time Points for both the Index ($\chi^2 = 8.824$; $p = 0.0121$) and Little fingers ($\chi^2 = 11.698$; $p = 0.0029$). For the Index finger (Fig. 2A), CSE increased at Late RT (2.203 ± 0.288 mV) as compared to Early RT (1.800 ± 0.274 mV; $p = 0.0045$) and GoCue (1.838 ± 0.290 mV; $p = 0.0213$). CSE measured at Early RT and GoCue did not differ ($p = 0.6654$). For the Little finger (Fig. 2B), CSE decreased at Late RT (1.572 ± 0.253 mV) as compared to both Early RT (1.764 ± 0.278 mV; $p = 0.0261$) and GoCue (1.975 ± 0.330 mV; $p = 0.0006$). CSE also decreased from GoCue to Early RT ($p = 0.0294$). Overall, these results show that CSE increased (or decreased) in a finger-*specific* manner during movement preparation in the ICF Experiment.

For the SICI Experiment, the CSE data (Fig. 2C–D) revealed an Incentives * Time Points * Initiating Finger interaction ($\chi^2 = 10.014$; $p = 0.0402$), which was decomposed by conducting simple effects of Time Points separately for each level of Incentives and Initiating Finger. Specifically, when the Index initiated sequences (Fig. 2C), the results revealed simple effects of Time Points in the Reward ($\chi^2 = 10.470$; $p = 0.0053$), Neutral ($\chi^2 = 8.908$; $p = 0.0116$) and Punishment conditions ($\chi^2 = 12.580$; $p = 0.0019$). Across all Incentive conditions, CSE was greater at Late RT (2.667 ± 0.132 mV) as compared to both GoCue (1.980 ± 0.081 mV; $p = 0.0011$) and Early RT (1.747 ± 0.081 mV; $p < 0.0001$). CSE at Early RT was also lower than at GoCue ($p = 0.0247$). Oppositely, when the Little finger initiated sequences (Fig. 2D), the results revealed no simple effects of Time Points in the Reward ($\chi^2 = 3.368$; $p = 0.2784$), Neutral ($\chi^2 = 2.144$; $p = 0.3422$), and Punishment conditions ($\chi^2 = 4.512$; $p = 0.3144$). This shows that CSE did not differ between GoCue (1.854 ± 0.076 mV), Early RT (1.769 ± 0.059 mV) and Late RT (2.033 ± 0.103 mV). Overall, these results show that CSE increased in a finger-*specific* manner during movement preparation in the SICI Experiment.

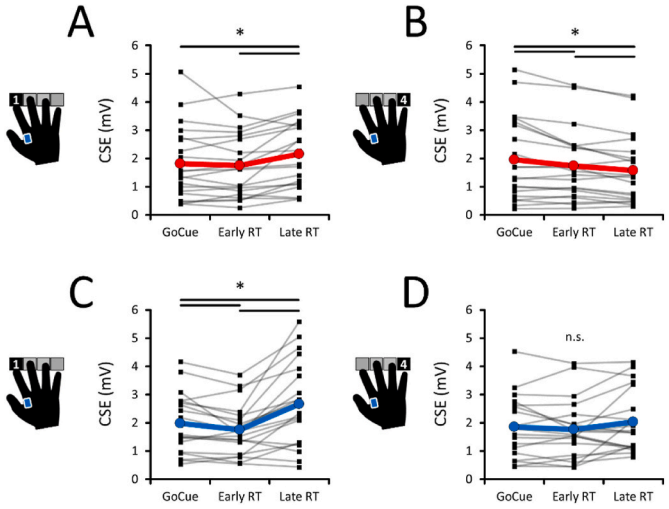

Fig. 2. Finger-*specific* CSE changes during movement preparation. CSE was measured in the FDI muscle only. **(A)** *ICF Experiment.* When the index initiated sequences, CSE increased as movement onset approached. **(B)** *ICF Experiment.* When the little finger initiated sequences, CSE monotonically decreased as movement onset approached. **(C)** *SICI Experiment.* When the index finger initiated sequences, CSE increased as movement onset approached. **(D)** *SICI Experiment.* When the little finger initiated sequences, CSE did not change as movement onset approached. For all panels, individual data (n = 20) with their respective means are shown [44].

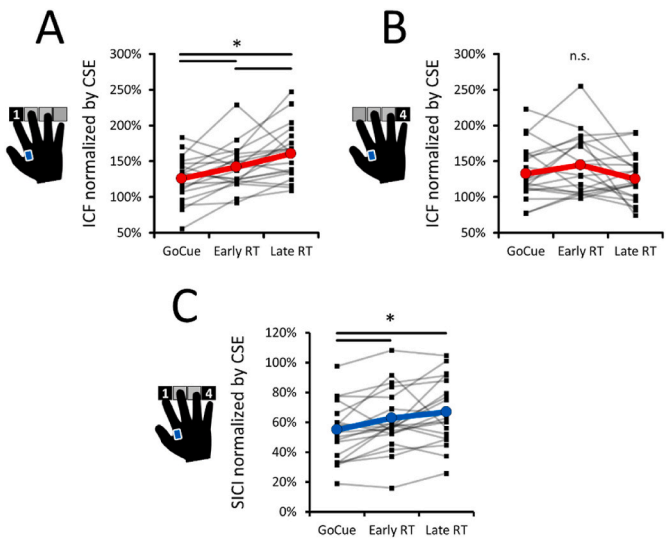

Fig. 3. Finger-*specific* ICF and finger-*unspecific* SICI changes during movement preparation. (A) *ICF Experiment.* When the index initiated sequences, ICF increased as movement onset approached. **(B)** *ICF Experiment.* When the little finger initiated sequences, ICF did not change as movement onset approached. **(C)** *SICI Experiment.* Regardless of whether the index or little finger initiated sequences, SICI decreased as movement onset approached. For all panels, individual data (n = 20) with their respective means are shown [44].

3.3. Finger-specific ICF increases and finger-unspecific SICI decreases during movement preparation

These analyses assessed if Time Points altered ICF and SICI during movement preparation. For the ICF Experiment (Fig. 3A and B), the ICF data revealed a Time Points * Initiating Finger interaction ($\chi^2 = 42.174$; $p < 0.0001$). A breakdown of this interaction revealed a simple effect of Time Points when the Index (Fig. 3A; $\chi^2 = 13.104$; $p = 0.0028$), but not when the Little finger (Fig. 3B; $\chi^2 = 4.786$; $p = 0.0914$), initiated sequences. For the Index finger, ICF was greater at both Late RT (162 ± 8%; $p = 0.0003$) and Early RT (145 ± 9%; $p = 0.0225$) as compared to GoCue (128 ± 8%). ICF was also greater at Late RT than at Early RT ($p = 0.0459$). For the Little finger, these results also show that ICF did not differ between GoCue (134 ± 8%), Early RT (145 ± 9%) and Late RT (126 ± 7%). Overall, these results show that ICF monotonically increased in a finger-*specific* manner during movement preparation.

For the SICI Experiment (Fig. 3C), the SICI data revealed an effect of Time Points ($\chi^2 = 20.023$; $p < 0.0001$), but no effect of Initiating Finger ($\chi^2 = 1.168$; $p = 0.2798$), no Time Points * Initiating Finger interaction ($\chi^2 = 1.552$; $p = 0.4602$), and no three-way Incentives * Time Points * Initiating Finger interaction ($\chi^2 = 7.554$; $p = 0.1094$). For Time Points, SICI decreased (greater MEP amplitude) at both Late RT (59 ± 5%; $p = 0.0001$) and Early RT (57 ± 5%; $p = 0.0098$) as compared to GoCue (50 ± 4%). SICI did not differ between Early and Late RT ($p = 0.5700$). Overall, these results show that SICI decreased in a finger-*unspecific* manner during movement preparation.

3.4. Incentives enhanced behavioural performance

Overall, the behavioural results show that TMS pulses disrupted performance by slowing RTs and MTs and – more importantly – that incentives robustly enhanced performance across all TMS Trial Types. In addition, the faster RTs and MTs within the Reward and Punishment conditions were not accompanied by decreases in Accuracy.

3.5. Behaviour from the ICF experiment

The RT data (Figs. 4A–5A) revealed an effect of Incentives ($\chi^2 = 213.402$, $p < 0.0001$), an effect of TMS Trial Types ($\chi^2 = 11.987$, $p = 0.0025$), but no Incentives * TMS Trial Types interaction ($\chi^2 = 1.455$, $p = 0.8345$). For Incentives (Fig. 4A), RTs were faster in both the Reward (552 ± 20 ms; $p < 0.0001$) and Punishment conditions (556 ± 20 ms; $p < 0.0001$) as compared to Neutral (587 ± 20 ms). RTs did not differ between the Reward and Punishment conditions ($p = 0.0813$). For TMS Trial Types (Fig. 5A), RTs slowed on ICF (585 ± 22 ms) as compared to both CSE (561 ± 20 ms; $p = 0.0027$) and NoTMS trials (550 ± 19 ms; $p = 0.0012$). RTs did not slow on CSE trials as compared to NoTMS trials ($p = 0.0980$). Overall, this shows that delivering ICF pulses during movement preparation slowed RT, but that rewards and punishments nonetheless successfully enhanced RT data across all TMS Trial Types.

The MT data (Figs. 4B–5B) revealed an effect of Incentives ($\chi^2 =$

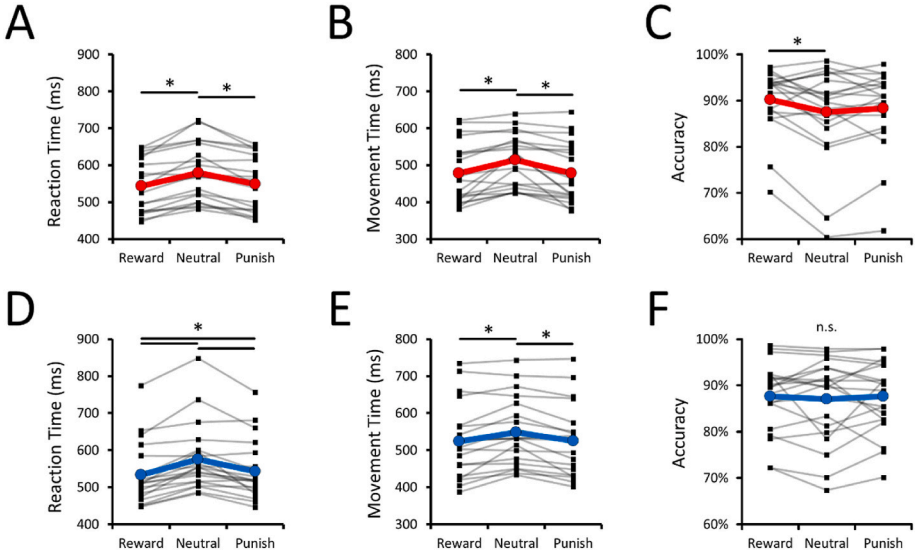

Fig. 4. Effect of rewards and punishments on performance. (A) *RT data from the ICF Experiment.* Rewards and punishments quickened RT as compared to neutral. **(B)** *MT data from the ICF Experiment.* Rewards and punishments quickened MT as compared to neutral. **(C)** *Accuracy data from the ICF Experiment.* Rewards improved accuracy as compared to neutral only. **(D)** *RT data from the SICI Experiment.* Rewards and punishments quickened RT as compared to neutral. **(E)** *MT data from the SICI Experiment.* Rewards and punishments quickened MT as compared to neutral. **(F)** *Accuracy data from the SICI Experiment.* No difference in accuracy was observed. For all panels, individual data (n = 20) with their respective means are shown [44].

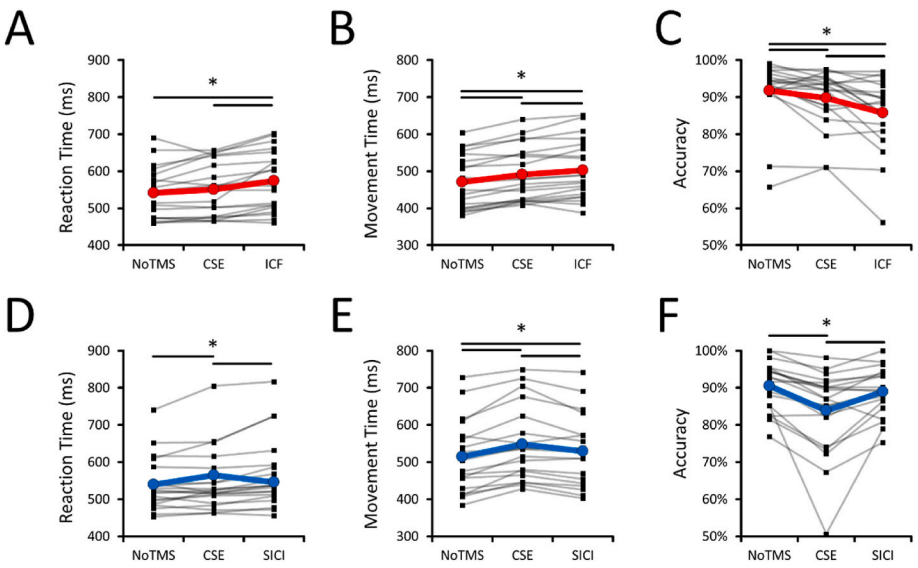

Fig. 5. Effect of TMS Trial Types (NoTMS, CSE, ICF or SICI) on performance. (A) *RT data from the ICF Experiment.* ICF trials slowed RT as compared to NoTMS and CSE. **(B)** *MT data from the ICF Experiment.* CSE and ICF trials slowed MT as compared to NoTMS. **(C)** *Accuracy data from the ICF Experiment.* CSE and ICF trials impaired accuracy as compared to NoTMS. **(D)** *RT data from the SICI Experiment.* CSE trials slowed RT as compared to NoTMS and SICI. **(E)** *MT data from the SICI Experiment.* CSE and SICI trials slowed MT as compared to NoTMS. **(F)** *Accuracy data from the SICI Experiment.* CSE trials impaired accuracy as compared to NoTMS and SICI. For all panels, individual data (n = 20) with their respective means are shown [44].

10.630; $p = 0.0049$), TMS Trial Types ($\chi^2 = 93.770$; $p < 0.0001$), and an Incentives * TMS Trial Types interaction ($\chi^2 = 11.830$, $p = 0.0187$). For Incentives (Fig. 4B), MTs were faster in both the Reward (486 ± 21 ms; $p = 0.0018$) and Punishment conditions (486 ± 21 ms; $p = 0.0022$) as compared to Neutral (520 ± 19 ms). MTs did not differ between the Reward and Punishment conditions ($p = 0.8651$). For TMS Trial Types (Fig. 5B), delivering ICF (511 ± 20 ms) slowed MT as compared to both CSE (501 ± 20 ms; $p = 0.0004$) and NoTMS trials (481 ± 20 ms; $p < 0.0001$). Delivering CSE also slowed MT as compared to NoTMS trials ($p < 0.0001$). Breakdown of the Incentives * TMS Trial Types interaction revealed simple effects of Incentives for NoTMS ($\chi^2 = 11.436$; $p = 0.0033$), CSE ($\chi^2 = 14.174$; $p = 0.0008$), and ICF trials ($\chi^2 = 6.142$; $p = 0.0464$), confirming that rewards and punishments enhanced MT across all TMS trial types. Overall, this shows that TMS pulses delivered during preparation slowed MT, but that rewards and punishments nonetheless successfully enhanced MT data across all TMS Trial Types.

The Accuracy data (Figs. 4C–5C) revealed an effect of Incentives ($\chi^2 = 11.683$, $p = 0.0029$), an effect of TMS Trial Types ($\chi^2 = 54.787$, $p < 0.0001$), but no Incentives * TMS Trial Types interaction ($\chi^2 = 7.346$, $p = 0.1187$). For Incentives (Fig. 4C), Rewards increased Accuracy (92 ± 1%) as compared to Neutral (90 ± 2%; $p = 0.0021$). Punishments (91 ± 1%) did not alter Accuracy as compared to the Reward ($p = 0.1389$) and Neutral conditions ($p = 0.0936$). For TMS Trial Types (Fig. 5C), Accuracy was higher on both NoTMS (93 ± 1%; $p < 0.0001$) and CSE trials (91 ± 1%; $p < 0.0011$) as compared to ICF ones (88 ± 2%). Accuracy was also lower on NoTMS as compared to CSE trials ($p = 0.0084$). Overall, these results show that rewards and punishments did not alter accuracy and that it was the highest on NoTMS trials.

3.6. Behaviour from the SICI experiment

The RT data (Figs. 4D–5D) revealed an effect of Incentives ($\chi^2 = 30.249$, $p < 0.0001$), an effect of TMS Trial Types ($\chi^2 = 12.627$, $p = 0.0018$), but no Incentives * TMS Trial Types interaction ($\chi^2 = 1.812$, $p = 0.7703$). For Incentives (Fig. 4D), RTs were faster in both the Reward (546 ± 24 ms; $p < 0.0001$) and Punishment conditions (555 ± 23 ms; $p = 0.0019$) as compared to Neutral (588 ± 26 ms). RTs did not differ between the Reward and Punishment conditions ($p = 0.0903$). For TMS Trial Types (Fig. 5D), RT decreased on CSE (581 ± 27 ms) as compared to SICI (559 ± 24 ms; $p = 0.0006$) and NoTMS trials (550 ± 21 ms; $p = 0.0033$). RTs on NoTMS and SICI trials did not differ ($p = 0.1461$). Overall, this shows that delivering TMS pulses during preparation slowed RT, but that rewards and punishments nonetheless successfully enhanced RT data across all TMS Trial Types.

The MT data (Figs. 4E–5E) revealed an effect of Incentives ($\chi^2 = 9.752$; $p = 0.0076$) and TMS Trial Types ($\chi^2 = 114.934$; $p < 0.0001$), but no Incentives * TMS Trial Types interaction ($\chi^2 = 0.911$; $p = 0.9230$). For Incentives (Fig. 4E), MTs were faster in both the Reward (535 ± 27 ms; $p = 0.0092$) and Punishment conditions (535 ± 26 ms; $p = 0.0027$) as compared to Neutral (558 ± 24 ms). MTs did not differ between the Reward and Punishment conditions ($p = 0.9927$). For TMS Trial Types (Fig. 5E), MTs slowed when CSE (559 ± 25 ms; $p < 0.0001$) and SICI were delivered (542 ± 25 ms; $p < 0.0001$) as compared to NoTMS trials (526 ± 25 ms). MTs were also slower on CSE as compared to SICI trials ($p < 0.0001$). This shows TMS pulses delivered during preparation slowed MT, but that rewards and punishments nonetheless successfully enhanced MT data across all TMS Trial Types.

The Accuracy data (Figs. 4F–5F) revealed an effect of TMS Trial Types ($\chi^2 = 66.248$, $p < 0.0001$), but no effect of Incentives ($\chi^2 = 0.107$, $p = 0.9479$), and no Incentives * TMS Trial Types interaction ($\chi^2 = 7.210$, $p = 0.1252$). This shows that Accuracy did not differ between the Reward (88 ± 2%), Neutral (88 ± 2%) and Punishment conditions (88 ± 2%) Accuracy data for each level of Incentives is shown in Fig. 4F. For TMS Trial Types (Fig. 5F), Accuracy decreased on CSE (86 ± 2%) as compared to both NoTMS (92 ± 1%; $p < 0.0001$) and SICI trials (91 ± 2%; $p < 0.0001$). Accuracy also tended to be lower on SICI trials as compared to NoTMS ($p = 0.0658$). Overall, these results show that rewards and punishments did not alter accuracy and that it was the highest in NoTMS trials.

3.7. Punishments altered CSE in the SICI experiment, but not in the ICF experiment

These analyses assessed if Incentives altered CSE during movement preparation. For the ICF Experiment, the CSE data (Fig. 6A) revealed no effect of Incentives ($\chi^2 = 4.019$; $p = 0.1340$), no Incentives * Time Points ($\chi^2 = 5.903$; $p = 0.2065$), no Incentives * Initiating Finger ($\chi^2 = 2.167$; $p = 0.3383$), and no three-way interaction ($\chi^2 = 3.931$; $p = 0.4154$). For

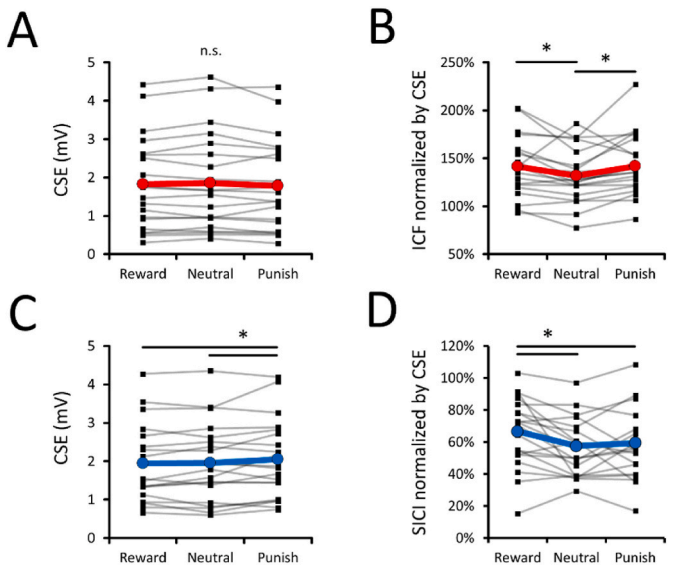

Fig. 6. Effects of rewards and punishments on CSE, ICF, and SICI during preparation. (A) *CSE data from the ICF Experiment.* No effect of rewards or punishments on CSE as compared to neutral. **(B)** *ICF data from the ICF Experiment.* Rewards and punishments both increased ICF as compared to neutral. **(C)** *CSE data from the SICI Experiment.* Punishments increased CSE as compared to rewards and neutral. **(D)** *SICI data from the SICI Experiment.* Rewards decreased SICI as compared to neutral and punishments. For all panels, individual data (n = 20) with their respective means are shown [44].

the ICF Experiment, this shows that CSE did not differ between the Reward (1.848 ± 0.277 mV), Neutral (1.891 ± 0.277 mV), and Punishment conditions (1.837 ± 0.277 mV).

For the SICI Experiment, the CSE data (Fig. 6C) revealed an effect of Incentives ($\chi^2 = 6.469$; $p = 0.0394$), but no Time Points * Incentives ($\chi^2 = 5.831$; $p = 0.2122$), and no Incentives * Initiating Finger interaction ($\chi^2 = 0.621$; $p = 0.7329$). For Incentives (Fig. 6C), CSE increased in Punishment (1.764 ± 0.221 mV) as compared to both the Reward (1.643 ± 0.206 mV; $p = 0.0306$) and Neutral conditions (1.655 ± 0.208 mV; $p = 0.0576$). CSE did not differ between the Reward and Neutral conditions ($p = 0.8055$). Overall, this shows that punishments increased CSE as compared to both the reward and neutral conditions in the SICI Experiment.

3.8. *Both rewards and punishments increased ICF, but only rewards decreased SICI*

These analyses assessed if Incentives altered ICF and SICI during movement preparation. For the ICF Experiment, the ICF data (Fig. 6B) revealed an effect of Incentives ($\chi^2 = 9.407$; $p = 0.0091$), but no Incentives * Time Points ($\chi^2 = 2.741$; $p = 0.6020$), no Incentives * Initiating Finger ($\chi^2 = 1.321$; $p = 0.5166$) and no three-way interaction ($\chi^2 = 6.742$; $p = 0.1502$). For Incentives (Fig. 6B), ICF increased in both the Reward (146 ± 7%; $p = 0.0075$) and Punishment conditions (145 ± 7%; $p = 0.0108$) as compared to Neutral (133 ± 6%). ICF in Reward and Punishment conditions did not differ ($p = 0.9022$). Overall, this shows that both rewards and punishments increased ICF as compared to the neutral condition. This also shows that the effects of Incentives on ICF did not statistically interact with Time Points or Initiating Finger, suggesting that incentives enhance performance by increasing GLUTergic

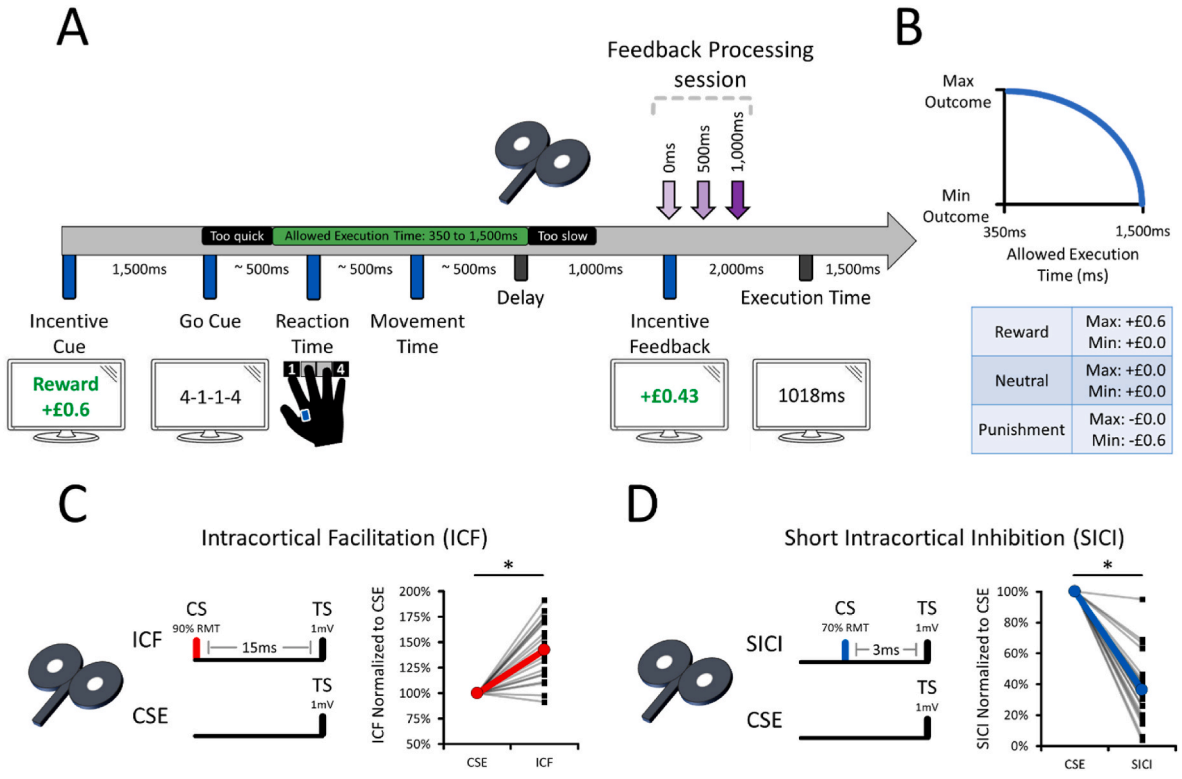

Fig. 7. Assessment of ICF and SICI during the Feedback Processing session. (A) *Chronology of a typical trial.* The same procedures as in Fig. 1 were used, except for the Time Points at which TMS pulses were delivered. TMS pulses were delivered either at Incentive Feedback Onset (FB Onset, or 0 ms), 500 ms or 1,000 ms later. EMG data were also recorded from the right FDI muscle (depicted as a blue electrode). **(B)** *The decay function used to adjust the incentives based on performance.* This procedure is identical to the one used in the Movement Preparation session. **(C)** *TMS parameters for the ICF Experiment (n = 20)* successfully induced ICF at rest, as assessed by delivering 30 single pulses and 30 paired ICF pulses. **(D)** *TMS parameters for the SICI Experiment (n = 20)* successfully induced SICI at rest, as assessed by delivering 30 single pulses and 30 paired SICI pulses. For panels (C) and (D), individual data with their respective means are shown [44]. RMT means resting motor threshold. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

activity in a temporal- and finger-*unspecific* manner during movement preparation.

For the SICI Experiment, the SICI data (Fig. 6D) revealed an effect of Incentives ($\chi^2 = 15.735$; $p = 0.0091$), but no Incentives * Time Points ($\chi^2 = 6.006$; $p = 0.1987$), no Incentives * Initiating Finger ($\chi^2 = 2.050$; $p = 0.3589$), and no three-way interaction ($\chi^2 = 7.554$; $p = 0.1094$). For Incentives (Fig. 6D), SICI decreased in Reward (60 ± 5%) as compared to both the Punishment (53 ± 4%; $p = 0.0015$) and Neutral conditions (52 ± 4%; $p = 0.0006$). SICI on Neutral and Punishment conditions did not differ ($p = 0.7990$). Overall, this shows that rewards decreased SICI as compared to both the punishment and neutral conditions. This also shows that the effects of rewards on SICI did not statistically interact with Time Points or Initiating Finger, suggesting that rewards enhance performance by decreasing $GABA_A$-mediated inhibition in a temporal- and finger-*unspecific* manner during movement preparation.

3.9. ICF and SICI data were not associated with RT data

To determine if the effect of Incentives in ICF and SICI data could be explained by the corresponding behavioural differences in RTs, the trial-per-trial association of RT with ICF or SICI data was explored using generalised mixed models. Specifically, the same analyses as above were conducted but also included RTs as a covariate to determine if RTs predicted ICF or SICI data. The results revealed that RTs did neither predict ICF ($\chi^2 = 0.940$; $p = 0.3323$) nor SICI data ($\chi^2 = 0.124$; $p = 0.7244$). This suggests that the incentive-induced differences in RTs do not account for the corresponding differences in ICF and SICI data.

4. Rational of the feedback processing session

The above results show that, as compared to the neutral condition, both rewards and punishments increased ICF, whereas only rewards decreased SICI during preparation. Interestingly, the results also revealed that these effects of Incentives on ICF and SICI were temporally- and finger-*unspecific*, as they did not interact with the finger-*specific* ICF increases and finger-*unspecific* SICI decreases observed as movement onset approached. This suggests that incentive-induced ICF and SICI changes reflect temporally unspecific mechanisms by which rewards and punishments alter M1's intracortical excitability to enhance performance, as previous TMS work would suggest [41,42,54]. If valid, one implication is that incentives enhance performance not by solely altering movement preparation, but by inducing a tonic brain state that permeates beyond movement preparation. The objective of this additional session was to evaluate this possibility.

Here, the effects of rewards and punishments on ICF and SICI during the processing of feedback (>1,000 ms after the execution of the sequences) were evaluated. The same experimental procedures as in Fig. 1 were used except for the Time Points at which TMS pulses were delivered. In this Feedback Processing session, TMS pulses were delivered at Feedback (FB) Onset as well as 500 ms and 1,000 ms after. If ICF and SICI during feedback processing are modulated similarly as in movement preparation, this would suggest that increased GLUTergic activity and decreased $GABA_A$-mediated inhibition are (tonic) temporally-*unspecific* mechanisms by which incentives enhance motor performance. Conversely, if ICF and SICI are not altered during feedback processing, this would suggest that rewards and punishments selectively alter ICF and SICI during movement preparation to enhance motor performance. Importantly, to strengthen the possibility that incentives could selectively alter movement preparation but not feedback processing, the same two groups of 20 participants that showed incentive-*specific* ICF and SICI changes during the Movement Preparation session were recruited for the Feedback Processing session.

5. Results – feedback processing session

5.1. ICF and SICI were reliably observed at rest

The same TMS parameters as in the Movement Preparation session were used in the Feedback Processing session (Fig. 7C and D). The results revealed significant M1 facilitation with ICF (Fig. 7C; 1.389 ± 0.167 mV) as compared to CSE (0.988 ± 0.123 mV; $p < 0.0001$). In addition, there was significant M1 inhibition with SICI (Fig. 7D; 0.379 ± 0.067 mV) as compared to CSE (1.089 ± 0.143 mV; $p < 0.0001$). This confirms that ICF and SICI were reliably observed at rest.

5.2. Incentives enhanced behavioural performance

Overall, the behavioural results show that incentives successfully enhanced motor performance without decreasing accuracy, replicating the results from the Movement Preparation session.

5.3. Behaviour from the ICF experiment

The RT data (Fig. 8A) revealed an effect of Incentives ($\chi^2 = 13.740$; $p = 0.0010$), which further revealed that RTs were faster on both the Reward (536 ± 15 ms; $p = 0.0004$) and Punishment conditions (540 ± 15 ms; $p = 0.0003$) as compared to Neutral (575 ± 18 ms). RTs did not differ between the Reward and Punishment conditions ($p = 0.1848$). This shows that rewards and punishments both enhanced RT data.

The MT data (Fig. 8B) revealed an effect of Incentives ($\chi^2 = 7.837$; $p = 0.0199$), which further revealed that MTs were faster on both the Reward (446 ± 19 ms; $p = 0.0095$) and Punishment conditions (449 ± 19 ms; $p = 0.0176$) as compared to Neutral (481 ± 18 ms). MTs did not differ between the Reward and Punishment conditions ($p = 0.3038$). This shows that rewards and punishments both enhanced MT data.

The Accuracy data (Fig. 8C) revealed no effect of Incentives ($\chi^2 = 1.697$; $p = 0.4281$), confirming that accuracy did not differ between the Reward (94 ± 1%), Neutral (94 ± 1%) and Punishment conditions (94 ± 1%).

5.4. Behaviour from the SICI experiment

The RT data (Fig. 8D) revealed an effect of Incentives ($\chi^2 = 24.930$; $p < 0.0001$), which further revealed that RTs were faster on both the Reward (534 ± 18 ms; $p < 0.0001$) and Punishment conditions (542 ± 20 ms; $p = 0.0061$) as compared to Neutral (579 ± 23 ms). RTs did not differ between the Reward and Punishment conditions ($p = 0.1141$). This shows that rewards and punishments both enhanced RT data.

The MT data (Fig. 8E) revealed an effect of Incentives ($\chi^2 = 7.840$; $p = 0.0198$), which further revealed that MTs were faster on both the Reward (498 ± 26 ms; $p = 0.0107$) and Punishment conditions (500 ± 25 ms; $p = 0.0080$) as compared to Neutral (555 ± 28 ms). MTs did not differ between the Reward and Punishment conditions ($p = 0.7768$). This shows that rewards and punishments both enhanced MT data.

The Accuracy data (Fig. 8F) revealed no effect of Incentives ($\chi^2 = 4.046$; $p = 0.1323$), confirming that accuracy did not differ between the Reward (95 ± 1%), Neutral (93 ± 1%) and Punishment conditions (94 ± 1%).

5.5. Incentives did not alter CSE in the ICF experiment, but punishments increased CSE in the SICI one

These analyses assessed if Incentives altered CSE during feedback processing. For the ICF Experiment, the CSE data (Fig. 9A) revealed no effect of Incentives ($\chi^2 = 3.490$; $p = 0.1747$), no effect of Time Points ($\chi^2 = 3.845$; $p = 0.1462$), and no Incentives * Time Points interaction ($\chi^2 = 1.714$; $p = 0.7882$). This shows that CSE did not differ between the Reward (1.944 ± 0.290 mV), Neutral (2.016 ± 0.304 mV), and Punishment (1.902 ± 0.304 mV) conditions.

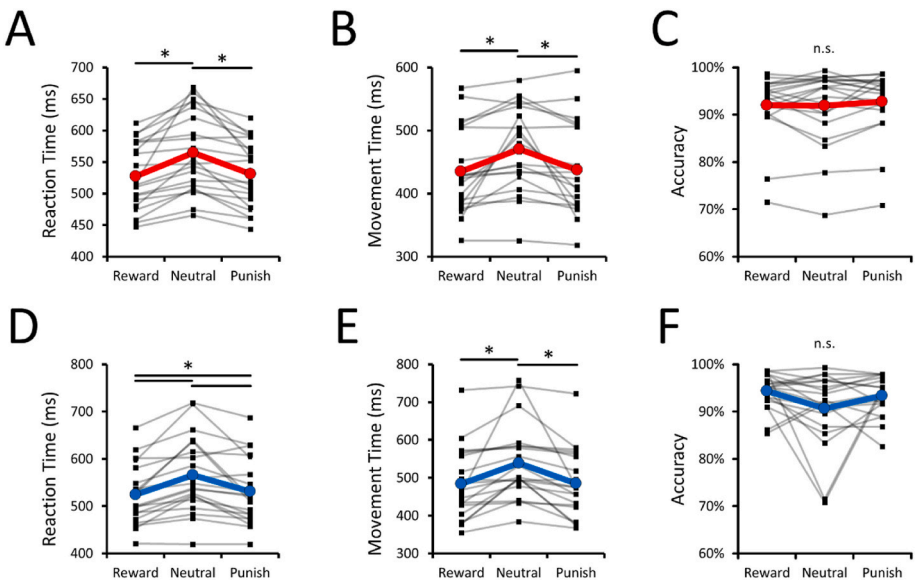

Fig. 8. Effect of rewards and punishments on performance. **(A)** *RT data from the ICF Experiment.* Rewards and punishments quickened RT as compared to neutral. **(B)** *MT data from the ICF Experiment.* Rewards and punishments quickened MT as compared to neutral. **(C)** *Accuracy data from the ICF Experiment.* No difference in accuracy was observed. **(D)** *RT data from the SICI Experiment.* Rewards and punishments quickened RT as compared to neutral. **(E)** *MT data from the SICI Experiment.* Rewards and punishments quickened MT as compared to neutral. **(F)** *Accuracy data from the SICI Experiment.* No difference in accuracy was observed. For all panels, individual data (n = 20) with their respective means are shown [44].

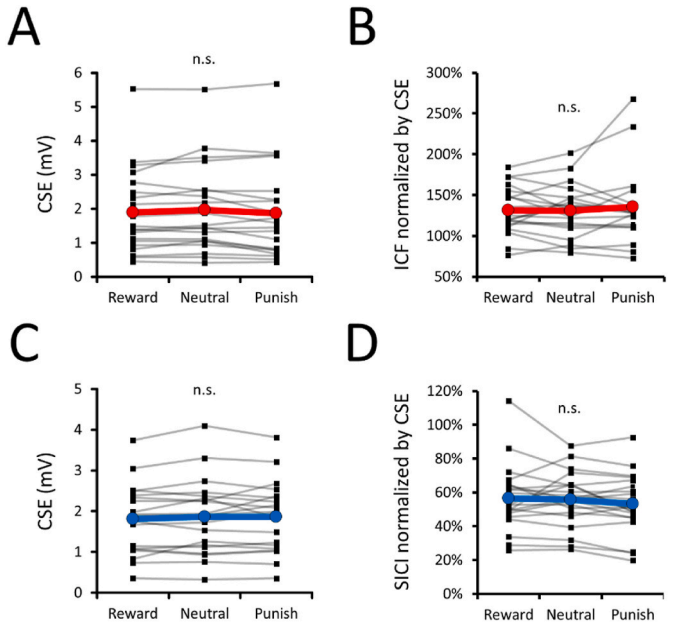

Fig. 9. Effects of rewards and punishments on CSE, ICF, and SICI during feedback processing. **(A)** *CSE data from the ICF Experiment.* No effect of rewards or punishments on CSE as compared to neutral. **(B)** *ICF data from the ICF Experiment.* No effect of rewards or punishments on ICF as compared to neutral. **(C)** *CSE data from the SICI Experiment.* No effect of rewards or punishments on CSE as compared to neutral. **(D)** *SICI data from the SICI Experiment.* No effect of rewards or punishments on SICI as compared to neutral. For all panels, individual data (n = 20) with their respective means are shown [44].

For the SICI Experiment, the CSE data (Fig. 9C) revealed an Incentives * Time Points interaction ($\chi^2 = 22.973$; $p = 0.0001$) and an effect of Time Points ($\chi^2 = 17.670$; $p = 0.0001$), but no effect of Incentives ($\chi^2 = 3.225$; $p = 0.1994$). Note that only the effect of Incentives is shown in Fig. 9C, for consistency with the other panels. The Incentives * Time Points interaction was decomposed by conducting simple effects of Incentives at each level of Time Points.

At FB Onset, despite results revealing a simple effect of Incentives ($\chi^2 = 5.762$; $p = 0.0561$), CSE did not differ in the Reward (1.963 ± 0.104 mV; $p = 0.9361$) and Punishment conditions (1.869 ± 0.105 mV; $p = 0.1032$) as compared to Neutral (1.959 ± 0.106 mV). CSE did not differ between the Reward and Punishment conditions ($p = 0.1086$). At 500 ms, the simple effect of Incentives ($\chi^2 = 8.206$; $p = 0.0165$) revealed greater CSE in Punishment (1.923 ± 0.105 mV) as compared to the Reward condition (1.782 ± 0.102 mV; $p = 0.0126$). Both the Reward ($p = 0.0837$) and Punishment conditions ($p = 0.2365$) did not differ from the Neutral one (1.875 ± 0.105 mV). At 1000 ms, the simple effect of Incentives ($\chi^2 = 10.796$; $p = 0.0045$) revealed greater CSE in Punishment (1.910 ± 0.105 mV) as compared to both the Reward (1.758 ± 0.102 mV; $p = 0.0024$) and Neutral conditions (1.824 ± 0.104 mV; $p = 0.0378$). CSE did not differ between the Reward and Neutral conditions ($p = 0.1507$). Overall, the absence of an effect of Incentives shows that CSE data were not systematically altered by rewards and punishments (Fig. 9C).

5.6. Incentives did not alter ICF or SICI during feedback processing

These analyses assessed if Incentives altered ICF and SICI during feedback processing. For the ICF Experiment, the ICF data (Fig. 9B) revealed no effect of Incentives ($\chi^2 = 0.859$; $p = 0.6508$), no effect of Time Points ($\chi^2 = 1.511$; $p = 0.4699$), and no Incentives * Time Points interaction ($\chi^2 = 5.508$; $p = 0.2391$). Overall, this shows that ICF did not differ between the Reward (135 ± 7%), Neutral (135 ± 8%) and Punishment conditions (142 ± 11%).

For the SICI Experiment, the SICI data (Fig. 9D) revealed no effect of Incentives ($\chi^2 = 3.342$; $p = 0.1881$), no effect of Time Points ($\chi^2 = 0.898$; $p = 0.6382$), and no Incentives * Time Points interaction ($\chi^2 = 3.077$; $p = 0.5451$). Overall, this shows that SICI did not differ between the Reward (57 ± 4%), Neutral (56 ± 4%) and Punishment conditions (53 ± 4%).

6. Discussion

This work investigated if rewards and punishments enhance motor

performance by altering ICF and SICI in the left M1 during the preparation of sequences initiated by either the index or little finger of the right hand. First, the results revealed that as movement onset approached, CSE and ICF increased selectively when the index finger initiated sequences, whereas SICI decreased when both the index and little fingers initiated sequences. These findings suggest that M1 increases CSE and GLUTergic activity in a finger-*specific* manner, whilst decreasing local $GABA_A$-mediated inhibition in a finger-*unspecific* manner during movement preparation. Second, rewards and punishments successfully quickened RTs and MTS as compared to the neutral condition in both sessions and Experiments, suggesting that incentives systematically enhanced motor performance. Third, both rewards and punishments increased ICF but only rewards decreased SICI during movement preparation. This suggests that both rewards and punishments recruit a common GLUTergic pathway, but that rewards recruit an additional (distinct) GABAergic pathway, in M1 to enhance motor performance. Finally, a control session showed that ICF and SICI were not modulated post-movement upon (and following) the delivery of reward and punishment feedback. This suggests that incentives enhance performance by altering M1's intracortical excitability during movement preparation only.

Finger-*specific* CSE and ICF increases, but finger-*unspecific* SICI decreases during movement preparation.

An important result of this study is that CSE increased during preparation in the finger that would initiate the cued finger-press sequence, as CSE increases were only observed in the FDI muscle when the index finger initiated sequences. These (index) finger-*specific* CSE increases replicate previous work (see Ref. [64]) and were observed in both the ICF and SICI Experiments, suggesting they reflect a robust feature of movement preparation. Here, two novel results are that M1 increased ICF as movement onset approached and that these ICF increases were also specific to when the index finger initiated sequences, suggesting that M1 increases its intracortical GLUTergic activity in a finger-*specific* manner during preparation. This finding aligns with anatomical work showing that projections from M1's GLUTergic pyramidal neurons are responsible for the preparation and execution of effector-*specific* motor commands [28,29]. Overall, this evidence suggests that the CSE increases observed during movement preparation are accompanied by increased ICF in M1, possibly reflecting increases in GLUTergic activity to prepare finger-*specific* motor commands.

Another key result is that SICI decreased in M1 as movement onset approached, which suggests that M1 decreases its local $GABA_A$-mediated inhibition during preparation. This finding aligns with – but importantly extends – existing TMS work [25–27] by showing that SICI measured from the FDI muscle decreased when both the index and little finger initiated sequences, suggesting that local $GABA_A$-mediated inhibition decreases in a finger-*unspecific* manner during preparation. Interestingly, when assessing these finger-*unspecific* SICI decreases, CSE increased selectively when the index finger initiated sequences, suggesting that CSE and SICI do not represent the same process. One possibility is that increases in CSE (and ICF) reflect upcoming finger-*specific* motor commands, whilst SICI decreases reflect the finger-*unspecific* local state transition from preparation to execution in M1 [65]. This contention is compatible with the status quo hypothesis [66–68]. Namely, this hypothesis posits that decreases in M1's beta-band power (13–30 Hz) – reflecting decreases in M1's $GABA_A$-mediated inhibition [69–71] – allow the current sensorimotor state to transition from preparation to execution. Anatomical evidence also supports that SICI changes should not be expected to be finger-*specific*, as local GABA interneurons have few [72], if any [73], corticospinal projections. Indeed, GABA interneurons locally regulate network dynamics of projecting GLUTergic pyramidal neurons [72,74], acting to shape the preparation (and execution) of motor commands [29,75] and/or withhold premature motor responses [64,76]. Overall, this evidence suggests that the present finger-*unspecific* SICI decreases during movement preparation do not reflect upcoming motor commands *per se*, but rather the locally GABAergic-regulated state transition from preparation to execution in M1.

6.1. Rewards and punishments both increased ICF during movement preparation

Both rewards and punishments quickened RTs and MTs without decreasing accuracy across both the ICF and SICI Experiments. These motor performance enhancements were also robust to the disruptive effects of TMS pulse delivery, confirming that incentives successfully enhanced motor performance.

In the ICF Experiment, rewards and punishments did not alter CSE as compared to the neutral condition during preparation, which contrasts with TMS work showing that rewarding stimuli increase CSE during preparation [6,7,10,77]. However, in the SICI Experiment, punishments increased CSE as compared to both rewards and neutral, which aligns with other TMS work showing that punishing stimuli increase CSE during preparation [8]. Although the exact reasons remain unclear, one possibility is that these previously reported CSE changes were driven by circuit-specific changes in M1, which the present study specifically investigated.

Here, a key novel result is that both rewards and punishments increased ICF during preparation as compared to neutral, suggesting that incentives upregulate M1's GLUTergic activity to enhance motor performance. Importantly, these ICF increases did not interact with the finger-*specific* ICF increases observed as movement onset approached, suggesting that rewards and punishments increase GLUTergic activity in a non-specific manner during preparation. First, this finding is largely consistent with animal work showing that the VTA quickly regulates M1's excitability [30] by increasing GLUTergic activity throughout the entire M1[31], suggesting a subcortical origin to the present ICF increases. Second, the finding that both incentives similarly increased ICF suggests that stimuli with positive (reward) and negative (punishment) motivational value recruit a common pathway in motor areas to guide behaviours (see Refs. [4,78,79] for further support). In support, Steel et al. (2019) showed that rewards enhance functional connectivity between the premotor cortex (PMC), striatum and cerebellum, whereas punishments enhance FC between the PMC and medial temporal lobe [79]. Although this suggests a network extending outside of cortical motor areas (see Ref. [80]), these results align with the present findings by suggesting that rewards and punishments recruit a common pathway in cortical motor areas. Overall, this evidence suggests that both rewards and punishments non-specifically increase M1's GLUTergic activity during movement preparation to enhance motor performance.

6.2. Only rewards decreased SICI during movement preparation

In contrast to ICF, rewards decreased SICI as compared to both punishment and neutral conditions during preparation, suggesting that rewards induce additional circuit-specific changes in M1 as compared to punishments. Similar to the ICF results, these SICI decreases did not interact with the finger-*unspecific* SICI decreases observed as movement onset approached, suggesting that rewards non-specifically release $GABA_A$-mediated inhibition in M1 during preparation. Assuming that reward-induced motor performance enhancements are driven by increased dopaminergic activity (although see Ref. [81]), one possibility is that the present SICI decreases were driven by dopaminergic pathways. On the one hand, VTA dopaminergic projections have been shown to enhance M1's excitability and crucially contribute to motor performance and learning (see Ref. [32] for a review), which could account for the present reward-specific SICI decreases. On the other hand, other evidence suggests that enhancing dopaminergic activity should rather increase SICI. For instance, activating M1's D2-like receptors using quinpirole has been shown to increase the excitability of M1's putative $GABA_A$ interneurons [34], suggesting increased $GABA_A$-mediated inhibition. Moreover, human TMS studies have shown that the

administration of dopamine agonists increases SICI (see Ref. [14] for a review), which also suggests increased $GABA_A$-mediated inhibition. Altogether, this evidence makes it unclear if rewards – assuming they increase dopaminergic activity – should increase or decrease SICI in M1, prompting an alternative interpretation.

Another possibility is that rewards decreased SICI by increasing noradrenergic activity. In support, M1 receives considerable noradrenergic innervation [82], and increases in noradrenergic activity are known to enhance the performance of goal-directed behaviours [83,84] as well as decrease SICI [14], suggesting that increased noradrenergic activity accounts for the present reward-specific SICI decreases. Since dopaminergic or noradrenergic activity was not measured in this study, a possible link between SICI and these pathways remains speculative. Nonetheless, a viable interpretation that remains is that rewards enhance performance by decreasing SICI during preparation, presumably facilitating the local transition from preparation to execution in M1 (as per the status quo hypothesis [66–68]). This interpretation also aligns with neuroimaging work showing that rewards improve performance by enhancing the widespread cortical representation of upcoming actions during preparation [85]. Finally, $GABA_A$-mediated inhibition is increasingly regarded as a key contributor to learning and memory consolidation [72,86], the selective effects of rewards on SICI may also explain the added value of rewards on motor learning and memory consolidation as compared to punishments [80,87–91]. Overall, the present SICI decreases suggest that rewards recruit a pathway ($GABA_A$-mediated inhibition) that is not recruited by punishments to enhance motor performance, presumably by facilitating the transition from preparation to execution in M1.

It should be noted that exploratory results showed that the enhancement of RTs by rewards and punishments was not associated with corresponding ICF and SICI changes. This result suggests that the effects of rewards and punishments on ICF and SICI during preparation cannot be explained by a quickening of RT. However, future studies should aim to replicate that finding, as the present results also showed that delivering TMS pulses over the left M1 disrupted motor performance in the right hand by slowing RTs and MTs. Since TMS perturbs M1 to obtain a measure of excitability, the demonstration of an unbiased association between motor performance and TMS-measured data is likely to be a challenge for future work.

6.3. Incentives did not alter ICF or SICI during feedback processing

During feeback processing, rewards and punishments enhanced motor performance in both the ICF and SICI Experiments. The results also revealed that CSE was not altered in the ICF Experiment, but that punishments enhanced CSE as compared to rewards in the SICI Experiment, which aligns with previous TMS work [54]. Here, an important result is that rewards and punishments did not alter ICF or SICI when measured post-movement during incentive feedback processing. This suggests that rewards and punishments enhance performance by altering M1's GLUTergic activity and $GABA_A$-mediated inhibition selectively during movement preparation. This result is consistent with the shift of activity from unexpected reward outcomes to predictive reward cues observed in VTA neurons [92], but contrasts with previous TMS work showing that rewards increase SICI upon reward delivery [41,42]. However, in these TMS studies, rewards were delivered randomly, suggesting that increases in SICI represented a prediction error (difference between expected and received outcome [93]) rather than the isolated effects of rewards on SICI in M1. Here, participants were provided incentive cues at the start of each trial and were *a priori* informed that incentives would be performance-contingent. Thus, participants likely combined knowledge of the incentive cues with their performance self-evaluation to anticipate the upcoming incentive feedback, resulting in little or no prediction errors. Such an absence of prediction errors could explain the present absence of ICF and SICI changes upon incentive feedback. Overall, these results show that rewards and punishments enhance performance by increasing ICF and decreasing SICI during movement preparation only. One implication is that targeting M1's GLUTergic and $GABA_A$-mediated activity during movement preparation – but not feedback processing – using pharmacological and/or non-invasive brain stimulation interventions can further enhance the neurorehabilitative potential of rewards in clinical settings [15–18].

6.4. Limitations

First, ICF and SICI were assessed in M1 only, making it unclear how the present results would extend to other brain areas (i.e., basal ganglia, cerebellum and frontal cortex) also known to process rewards and punishments [22,23]. Future work could evaluate corticocortical connectivity using dual-coil ppTMS [94] as well as combine TMS with electroencephalography [95] or magnetic resonance imaging [96] to evaluate how the present M1-specific results can be integrated into the brain network sensitive to valence.

Second, ICF and SICI are indirect assays of GLUTergic activity and $GABA_A$-mediated inhibition [14]. Other neural pathways, such as those activated by dopaminergic, noradrenergic, and $GABA_B$ agonist drugs, can also alter ICF and SICI measurements [14]. The extent to which these additional neural pathways contribute to the present results remains a query for future work.

Third, the TMS stimulation parameters were calibrated using the FDI cortical representation in the left M1, and all CSE, ICF, and SICI data were recorded from the right FDI only. As a result, the present finger-*specific* results can only be extended to movements performed with the index finger. Whether similar results could be obtained by stimulating other cortical representations (e.g., little finger muscle; abductor digiti minimi) remains unknown. Future studies will need to stimulate non-completely overlapping cortical representations [97] using different stimulation parameters (e.g., coil orientation) [98] to do so.

Finally, the time points used to deliver TMS pulses were fixed (as in Ref. [6]), whereas RTs typically display important within- and between-individual variability [99]. To ensure that TMS pulses delivered at different latencies during the RT period did not confound the present results, the TMS data were (re)pooled as a function of their delivery latency during the RT period (i.e., Early RT and Late RT). Doing so resulted in an average of ~50 valid TMS trials per level of Incentives and Time Points (see Tables 1 and 2), suggesting robust excitability estimates during movement preparation. To similarly control for TMS delivery latencies during the RT period, future studies could individualise TMS delivery time points by evaluating a baseline median RT or by iteratively calculating the median RT using a sliding window as the experiment progresses.

7. Conclusions

By measuring ICF and SICI from the right FDI muscle, the present results suggest that M1 increases its CSE and GLUTergic activity during the preparation of finger-*specific* movements. The results also suggest that M1 locally decreases its $GABA_A$-mediated inhibition in a finger-*unspecific* manner to transition from movement preparation to execution. Moreover, the results suggest that rewards and punishments both increased GLUTergic activity during preparation, suggesting that opposite incentives recruit a common pathway in M1 to enhance motor performance. Furthermore, rewards selectively decreased $GABA_A$-mediated inhibition during preparation, suggesting that rewards recruit an additional pathway to enhance performance. Similar results could not be found during feedback processing, suggesting that incentives alter M1's intracortical excitability selectively during movement preparation to enhance performance. Collectively, these results map the intracortical excitability changes in M1 by which incentives enhance motor performance.

CRediT authorship contribution statement

R. Hamel: Conceptualization, the project, designed the, Methodology, lead the, Investigation, collected, curated, Visualization, and, Validation, the data, performed the, Formal analysis, and wrote as well as revised the manuscript, also obtained a postdoctoral scholarship to financially support this project. **J. Pearson:** helped in leading the, Investigation, and collecting the data, also revised the manuscript. **L. Sifi:** helped in leading the, Investigation, and collecting the data. **D. Patel:** helped in leading the, Investigation, and collecting the data. **M.R. Hinder:** helped to, Conceptualization, the project, designed the, Methodology, also revised the manuscript. **N. Jenkinson:** provided, Resources, and supervised the project, also revised the manuscript.. **J.M. Galea:** Conceptualization, the project, designed the, Methodology, and provided the human and financial resources to support the project, also helped in, Validation, the data and in revising the manuscript.

Declaration of competing interest

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All authors agreed on the content of the manuscript prior to its submission to *Brain Stimulation*.

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