RESEARCH REPORT

Goal-directed modulation of stretch reflex gains is reduced in the non-dominant upper limb

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Abstract

Most individuals experience their dominant arm as being more dexterous than the non-dominant arm, but the neural mechanisms underlying this asymmetry in motor behaviour are unclear. Using a delayed-reach task, we have recently demonstrated strong goal-directed tuning of stretch reflex gains in the dominant upper limb of human participants. Here, we used an equivalent experimental paradigm to address the neural mechanisms that underlie the preparation for reaching movements with the non-dominant upper limb. There were consistent effects of load, preparatory delay duration and target direction on the long latency stretch reflex. However, by comparing stretch reflex responses in the non-dominant arm with those previously documented in the dominant arm, we demonstrate that goal-directed tuning of short and long latency stretch reflexes is markedly weaker in the non-dominant limb. The results indicate that the motor performance asymmetries across the two upper limbs are partly due to the more sophisticated control of reflexive stiffness in the dominant limb, likely facilitated by the superior goal-directed control of muscle spindle receptors. Our findings therefore suggest that fusimotor control may play a role in determining performance of complex motor behaviours and support existing proposals that the dominant arm is better supplied than the non-dominant arm for executing more complex tasks, such as trajectory control.

KEYWORDS
goal-directed, handedness, movement preparation, non-dominant, stretch reflex

1 | INTRODUCTION

Most people display significant arm dominance, often termed 'handedness', which can be expressed as superior reaction time, dexterity and strength in the dominant arm (Annett et al., 1979; Goble & Brown, 2008a; Shen & Franz, 2005). Hand movement performance variations have been related to differences in the neurological organization of the sensorimotor system. It was initially suggested that the observed asymmetries in motor behaviour

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Abbreviations: ANOVA, analysis of variance; EMG, electromyography; HSD, honest significant difference; LLR, long latency reflex; MEP, motor evoked potential; ROC, receiver operating characteristic; SLR, short latency reflex.

are related to the cortical hemisphere controlling movement of the arm (Liepmann, 1908). Later studies have demonstrated that both hemispheres contribute significantly to the control of contralateral goal-directed movements (Fisk & Goodale, 1988; Haaland & Harrington, 1989; Winstein & Pohl, 1995), although it has more recently been proposed that the left hemisphere in right-handers plays a specialized role in the control of complex ipsilateral and contralateral movements (Haaland & Harrington, 1996).

The hand dominance displayed by humans has led to a more specific theory of lateralization of motor control processes (Sainburg, 2005, 2014; Sainburg & Kalakanis, 2000). This proposal suggests that the dominant arm is primarily controlled through feedforward control of trajectory with accurate internal models of limb dynamics, whereas the non-dominant arm is primarily controlled through impedance control for stabilization. Such a theory can nicely explain why we might choose specific hands for certain tasks during bimanual object manipulation. For example, when unscrewing the lid of a jar, people will often hold (stabilize) a jar with their non-dominant hand and use the dominant hand to open the lid. Similarly, when threading a needle, the non-dominant hand might stabilize the needle while the dominant hand provides the fine manipulation of the thread. Indeed, it has been shown that, in certain contexts, the non-dominant arm exhibits more effective load compensation responses than the dominant limb (Bagesteiro & Sainburg, 2003). It has been suggested that such limb dominance might reflect differences in the hemispheric control of the body, where each hemisphere is specialized for different but complementary functions: the dominant system for controlling limb trajectory dynamics and the non-dominant system for controlling limb position (Sainburg, 2005).

Most of us routinely rely on the dominant arm to perform more complex and demanding motor tasks, but the mechanisms enabling the superior motor performance of the dominant limb are unclear. Little attention has been directed to whether differences in dexterity across the arms can partly represent differences in the goal-directed control of stretch reflexes. A better understanding of the motor asymmetry across the two arms might provide key insight into core sensorimotor principles. Recent evidence has shown that muscle spindle firing is highly task or goal dependent (e.g., Dimitriou, 2016; Papaioannou & Dimitriou, 2021; Ribot-Ciscar et al., 2009). However, postural studies of reflex modulation have found little or no lateralization or specialization of stretch reflex responses between the two limbs (Maurus et al., 2021; Walker & Perreault, 2015). Nevertheless, there is evidence that posture and movement exhibit different control strategies

(Kurtzer et al., 2005; Scheidt & Ghez, 2007). Moreover, it has been shown that both proprioceptive stretch reflexes and visuomotor feedback responses are selected according to the upcoming movement (Ahmadi-Pajouh et al., 2012; Česonis & Franklin, 2022; De Comite et al., 2021; Maeda et al., 2021; Wagner & Smith, 2008).

It has long been shown that long latency stretch reflexes exhibit task-dependent and goal-directed modulation (Akazawa et al., 1983; Crago et al., 1976; Hammond, 1956; Kimura et al., 2006; Nashed et al., 2014; Pruszynski et al., 2008). However, our recent work has shown that sufficient preparation time allows the goal-directed tuning of both short latency reflex (SLR) and long latency reflex (LLR) responses of the dominant upper limb (Papaioannou & Dimitriou, 2021; Torell et al., 2023). Here, we hypothesize that lateralization of independent fusimotor control might affect the goal-directed modulation of stretch reflexes in the non-dominant limb. That is, we predict that some of the behavioural differences resulting from limb dominance may reflect differences in the control of the gamma motor neuron system, which would result in differences in the goal-directed modulation of stretch reflexes. We test this hypothesis by examining the preparatory goal-directed tuning of stretch reflex gains in the non-dominant upper limb. We use a delayed-reach (centre-out) task to examine the stretch reflex responses of the non-dominant arm under different background loads and preparatory delays and compare the observed levels of goal-directed tuning with those previously documented for the dominant limb. That is, the current study was specifically designed to reveal whether the non-dominant arm displayed similar benefits of assistive loading and sufficient preparation time as means to promote the goal-directed tuning of stretch reflex gains, as shown previously to be the case for the dominant limb (Torell et al., 2023).

2 | MATERIALS AND METHODS

2.1 | Participants

For the purposes of the current study, the inclusion criteria required the participants to be 18–40 years old, right-handed, neurologically healthy, 165–185 cm in height and having normal movement range. We recorded muscle activity from the non-dominant left arm of 16 individuals (mean age 26.8 years, SD 6.4 years; 8 were female). All participants gave informed, written consent prior to participating in the study, per the Declaration of Helsinki. This experiment was part of a research programme approved by the Ethics Committee of Umeå University, Umeå, Sweden. All participants were

financially compensated for their contribution to this study. The current study also contrasted equivalent muscle responses previously recorded from the right dominant arm of 14 additional individuals (Torell et al., 2023). The inclusion criteria were the same for both groups. Although using two groups of right-handed participants to assess the impact of handedness on reflex tuning could be conceived as potentially limiting in terms of statistical power, we have no reason to believe that our two random population samples differed in an important way in terms of their 'right-handedness'. In addition, as described below in more detail, we have also assessed goal-directed tuning of reflexes using within-muscle metrics.

2.2 | Robotic platform

To perform the recordings from the left non-dominant arm, each participant sat upright in a customized chair that was mechanically stabilized to the floor. The participants were seated so that their elbow angle was 90°, and their shoulder joint was abducted approximately 45° as a starting position at the origin. The origin was located 20 cm in front of the participant. The chair was placed in front of a Kinarm™ robotic platform (Kinarm end-point robot, BKIN Technologies Ltd., Canada). The participants used their left hand to grasp the left handle of a bimanual robotic manipulandum (Figure 1). Their forearm was placed inside a customized foam-cushioned glove structure made of hard plastic material and secured in this structure using a leather fabric with Velcro attachments. The attachment ensured a tight mechanical connection between the participant's forearm, the plastic structure and the robotic handle. In addition, the glove ensured that the wrist supination/pronation was at a 0° angle. Velcro attachments were also used to secure an airsled to the plastic structure enveloping the forearm. The airsled allowed frictionless movement of the arm in a 2D plane. The robotic platform recorded kinematic data and sensors inside the handle (six-axis force transducer; Mini40-R, ATI Industrial Automation, USA) recorded forces exerted by the participants' hand. Kinematic and force data from the Kinarm platform were sampled at 1 kHz. The same set-up with the right handle was previously used for generating equivalent data from the dominant right arm of a separate group of participants (Torell et al., 2023).

2.3 | Experimental design

All visual stimuli were projected on a one-way mirror that otherwise occluded view of the hand and robotic handle (Figure 1a). Four orange circle outlines ('targets';
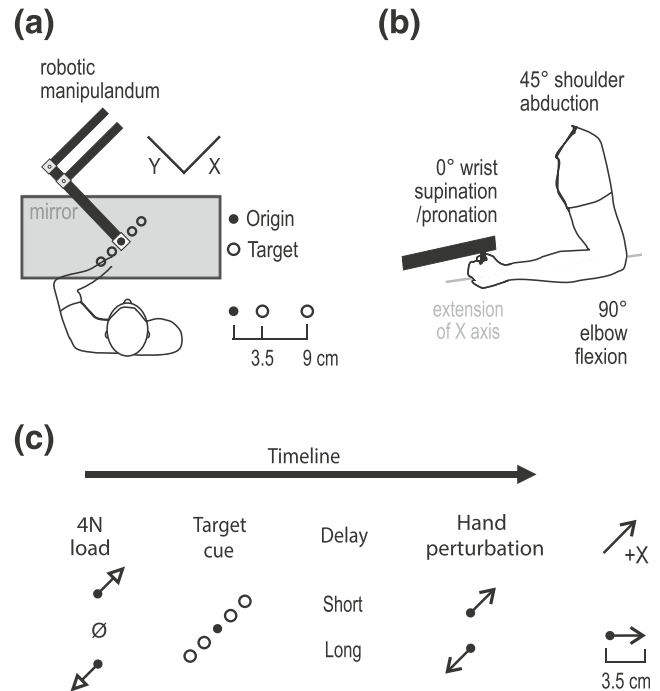
FIGURE 1 The robotic platform and experimental set-up (a). The participants were seated in an adjustable chair placed in front of the robotic platform. The participant's non-dominant left hand grasped a robotic handle. All visual stimuli were projected onto a one-way mirror. The participant could not view their hand or the robotic handle in this set-up. The position of the hand was represented by a white cursor. Four visual targets were continuously displayed along the X-axis. Two 'near' and two 'far' targets were used, placed at 3.5 and 9 cm from the origin, respectively. (b) Different view of the left arm in the starting position; the X-axis passes through the elbow joint. (c) In this experiment, each trial was initiated when the participant brought the cursor to the origin. A slow-rising 4-N load in either the +X (upper right direction) or −X direction (lower left direction) or a 'null' load (no load) was then applied. Regardless of load, the participant had to keep the hand at the origin. One of the four targets was then cued by turning red. The target remained in the cued state for either 250 or 750 ms. This preparatory delay was followed by a rapid position-controlled perturbation of the hand (3.5 cm in 150 ms) in either the −X or +X direction. The cursor position was frozen during the perturbation. At the end of the perturbation, the target turned green ('Go' signal), and the participant had to swiftly move the hand to the target.

2.4 cm diameter) and a circle outline representing the origin (1.3 cm diameter) were situated along the X-axis (as defined in Figure 1a). The line corresponding to X passes through the elbow joint. The centre-to-centre distance between the origin and the two 'near' targets was 3.5 cm, and the distance between the origin and the two 'far' targets was 9 cm. Hand position was represented by a white dot ('cursor'; 1 cm diameter). To start a new trial, the participant had to move the white cursor to the

origin. There, they had to remain immobile for a random wait period of 1–1.5 s. Provided that they had remained immobile inside the origin, the robotic manipulandum then generated a slow-rising 4-N load in either the +X or −X direction or no such pre-load was produced (Figure 1b). Any slow-rising load had a rise-time of 800 ms and a hold-time of 1200 ms.

At the end of this hold-time, and if the cursor remained immobile inside the origin, one of the four targets was cued by turning into a filled red circle and the target remained in this cued state for a relatively short (250 ms) or long time period (750 ms). At the end of this preparatory delay, a position-controlled haptic perturbation was delivered in either the +X or −X direction (3.5 cm of displacement, 150 ms of rise-time and no hold). That is, the hand was perturbed towards or away from the cued target. The cursor position was frozen for the duration of the perturbation. The haptic perturbations were designed to induce kinematics of a fast naturalistic point-to-point movement; that is, the resulting velocity profiles were approximately bell shaped. To achieve the desired hand kinematics on each trial, the robotic platform was allowed to apply the appropriate stiffness with as maximum of ∼40,000 N/m, regardless of load/force conditions. Although some of the imposed length change due to the perturbation might have occurred in tendon rather than muscle fascicles, the size of our perturbations and the stereotypical timeframe of the generated SLR and LLR (see Section 3) confirm that a substantial portion of the imposed length changes occurred in muscle and, thus, allowed us to assess the tuning of muscle stretch reflexes in the context of delayed reach. Once the mechanical perturbation ended (i.e., 150 ms after perturbation onset), the filled red circle (i.e., cued target) turned green, representing the 'Go' signal to reach the target. The participants were instructed to swiftly bring the cursor to the highlighted target.

After reaching the target, the participants were required to keep the hand at the target for 300 ms. Thereafter, the participants received visual feedback on the performance on this specific trial. The visual feedback was 'Too Slow' if the time between the onset of the 'Go' signal and the time the cursor entered the highlighted target was >1200 ms, 'Correct' if the target was reached after 400–1200 ms and 'Too Fast' if the target was reached after <400 ms. The selected feedback intervals encouraged the participant to move swiftly to the target, while allowing enough time for reaching the far target even when the hand had been perturbed in the opposite direction. The feedback message was visible for 300 ms. The participant then returned the cursor to the origin to initiate the next trial. If the participant wanted a break, they could move their hand to the side, instead of returning to the origin circle. Breaks were normally encouraged every two blocks of trials, where a 'block' represents one set of the 48 unique trials. Breaks normally lasted <5 min. The experiment contained 48 unique trial types: 4 targets (two directions and two distances) × 3 load conditions (slow-rising 4 N in the +X direction, −X direction or null) × 2 delays (250 and 750 ms) × 2 perturbation directions (+X and −X). There were 15 repetitions of each trial type (i.e., total number of trials was 720), and the trials were presented in a block-randomized manner. Each experiment took approximately 1.5 h to complete. The data recorded using this experimental design were analysed separately in the current study but also contrasted with previously recorded data from the dominant right arm. The data from the dominant right arm were generated using a mirror-equivalent version of experiment described above (Torell et al., 2023).

2.4 | Electromyography (EMG)

Surface EMG electrodes (Bagnoli™ DE-2.1, Delsys Inc., USA) were placed on the belly of seven muscles: (1) *m. brachioradialis*, (2) *m. biceps* brachii, (3) *m. triceps brachii caput laterale*, (4) *m. triceps brachii caput longum*, (5) *m. deltoideus pars anterior*, (6) *m. deltoideus pars posterior* and (7) *m. pectoralis major*. For the pectoralis in particular, the electrode was placed along the midclavicular line at approximately the height of the axilla. Prior to electrode placement, the skin was cleaned using alcohol swabs and the electrodes were coated with conductive gel. The electrodes were secured using surgical tape. The ground electrode had a diameter of 5.08 cm (Dermatrode® HE-R Reference Electrode type 00200-3400; American Imex, Irvine, CA, USA) and was placed on the *processus spinosus* of C7 region. The EMG signals were band-pass filtered online through the EMG system (20–450 Hz) and sampled at 1.0 kHz.

2.5 | Data pre-processing

Data pre-processing was performed using MATLAB® (version R2020b, MathWorks, Natick, MA, USA). EMG data were high pass filtered using a fifth-order, zero-phase-lag Butterworth filter with a 30-Hz cut-off and then rectified. Movement onset of each trial was defined as the time when 5% peak velocity was reached. The EMG data were normalized (z-transformed) to allow for comparisons of separate muscles and participants. The procedure to z-transform the data has been described in detail elsewhere (Dimitriou, 2014, 2016, 2018). In short, the z-transformation is performed by concatenating all EMG

data from one muscle (including activity during voluntary movement) and calculating a grand mean and grand standard deviation across all raw data, that is, generating a pair of these values for each individual muscle of each participant. Each muscle's grand mean is then subtracted from the measured EMG values that are then divided by the grand standard deviation. An additional EMG normalization approach was used to further evaluate reflex tuning differences between the dominant and non-dominant arms. This approach involved producing the average (mean) unnormalized EMG trace across repetitions of a trial type (aligned on perturbation onset) for each separate muscle/participant. For each muscle, the maximal EMG value across all averaged traces (i.e., across all trial types) observed anytime 50 ms after perturbation onset was used to normalize the raw EMG data as a proportion (%) of this value. As described in Section 3, equivalent statistical results were obtained regarding differences in reflex tuning between the dominant and non-dominant arms, regardless if the %-normalized or z-normalized approach was used.

Throughout, the first five blocks of trials were viewed as familiarization trials and were not included in the subsequent analyses. For each participant, data were averaged for each trial type for plotting and statistical analyses. For plotting purposes only, signals were smoothed using a 5-ms moving window. The data pre-processing procedures were identical to those previously used with regard to the right dominant arm (Torell et al., 2023). In addition to investigating the reflex modulation of the non-dominant arm, the current study also compared the goal-directed tuning of reflexes between the non-dominant (left) and dominant (right) upper limbs. Data from the dominant right arm were generated in a previous study, where a separate group of participants performed the mirror-equivalent experiment to the current one using their right dominant arm (Torell et al., 2023). Because target direction was the primary factor shaping reflex gains in both the dominant and non-dominant arms, the data used for these specific analyses were collapsed across target distances, so that 'goal' only represented target direction. To produce a measure that is more directly representative of goal-dependent tuning, the responses observed when preparing to stretch the homonymous muscle (i.e., trials where reaching the target required lengthening of the muscle) were subtracted from the responses observed when preparing to shorten the homonymous muscle.

2.6 | Statistical analyses

Statistical analyses were performed using z-normalized EMG data, available at Mendeley Data, V1, doi: 10.17632/4s28xcr6n6.1 (Torell et al., 2022). As the scope of

the study was to investigate goal-directed tuning of stretch reflex responses, the analyses mainly focused on EMG data from shoulder muscles, previously shown to exhibit stronger goal-directed tuning (vs. elbow) for an equivalent delayed-reach paradigm. However, some analyses of stretch reflexes from elbow muscles are also presented for comparison. Across participants, we generated median EMG values for three predetermined epochs: the pre-perturbation epoch (25 ms period prior to perturbation onset), the SLR epoch (25–50 ms period after perturbation onset) and the LLR epoch (75–100 ms after perturbation onset). Specifically, the analysed data contained the median EMG signal for each trial (i.e., median of each load, delay and target combination), for each muscle and participant in the three aforementioned epochs. To study the main and interaction effects of the non-dominant arm, the median EMG data were used to perform repeated-measures analysis of variance (ANOVA) of the design 2 (delay) × 3 (load) × 2 (target distance) × 2 (target direction), separately for each muscle type. For the SLR response in particular, ANOVA was conducted without including the pre-loaded ('loaded') muscle condition as it is known that automatic gain-scaling accompanying pre-loading tends to saturate the SLR response, preventing its goal-directed modulation (as occurred in our study; e.g., Figures 3 and 4). Post hoc analyses were performed using Tukey's honest significant difference (HSD). To check normality, Shapiro–Wilk's test for samples with <50 data points and Lilliefors' test for larger samples were used. Statistical comparisons of reflex responses between the dominant and non-dominant limbs were conducted with independent t-tests. All statistical analyses were performed using STATISTICA® (StatSoft Inc., USA).

The onset of SLR modulation was estimated using receiver operating characteristic (ROC) technique (Green & Swets, 1966). The ROC area is a value that assesses the overall performance of a binary classifier, where an ROC area of 1 and 0 represents perfect discrimination and an ROC area of .5 represents a discrimination performance equal to chance. As the differences between the target directions were stronger for the longer preparatory delay, we used these data for the ROC analysis. Specifically, the EMG curves of targets in the direction of homonymous muscle stretch were contrasted to EMG curves of targets in the direction of muscle shortening. Averages across target distance were viewed as representative of the reflex modulation in the population. In accordance with the results of Corneil et al. (2004), the discrimination was viewed as significant when the ROC area remained >.75 for five consecutive time periods (i.e., for at least 5 ms). To assess individual reflex modulation onset, a similar approach was used on individual

EMG responses across trials. This was done separately for each participant. To eliminate the risk of false positives, each SLR modulation onset was confirmed by visual inspection. The ROC curves were created using MATLAB® (version R2020b, MathWorks).

3 | RESULTS
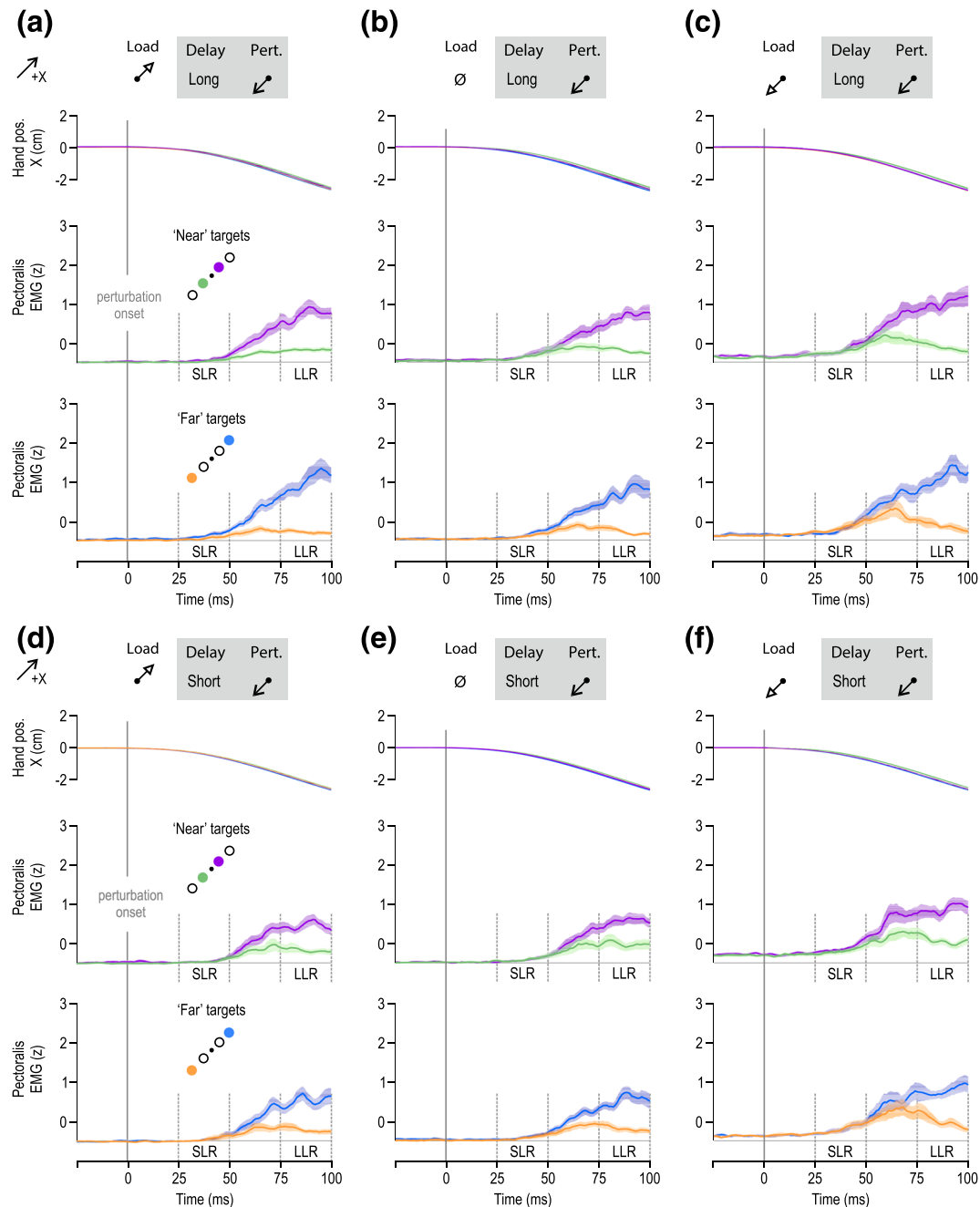
3.1 | The non-dominant arm

Sixteen participants were recruited to perform a delayed-reach task using their non-dominant left arm. On each trial, one of three different loads was applied (−4, 0 or 4 N), and the participants had to maintain their hand positioned inside the origin regardless. One of four targets was then cued (turned red), and after either a short or long preparatory delay, the left hand was perturbed by 3.5 cm in one of two directions (+X or −X; Figure 1). At the end of the haptic perturbation, the colour of the cued target changed from red to green, indicating to participants that they need to actively reach the cued target. This experiment examines how the target location (direction and distance), background load and delay between the presentation of the target and the perturbation impact reflex responses during reach preparation.

Figure 2 illustrates responses from the pectoralis muscle of a single participant. Visual inspection of the figure points to clear differences in EMG as a function of target direction during the LLR epoch (75–100 ms). However, there is no clear differentiation of EMG as a function of target direction during the SLR epoch (25–50 ms). Figures 3 and 4 represent equivalent averaged responses across all 16 participants, for the pectoralis and posterior deltoid, respectively. In contrast to what we have observed for the dominant right arm (Torell et al., 2023), our current figures and analyses indicate that goal-directed tuning of SLR responses was not prevalent in the non-dominant left arm. Specifically, in what follows, we first examine the impact of target location, load and delay on reflex responses of the left arm and then compare the level of goal-directed tuning of reflexes in the left and right arms. The statistical analyses confirm our initial hypothesis of reduced goal-directed tuning of stretch reflexes in the non-dominant upper limb.
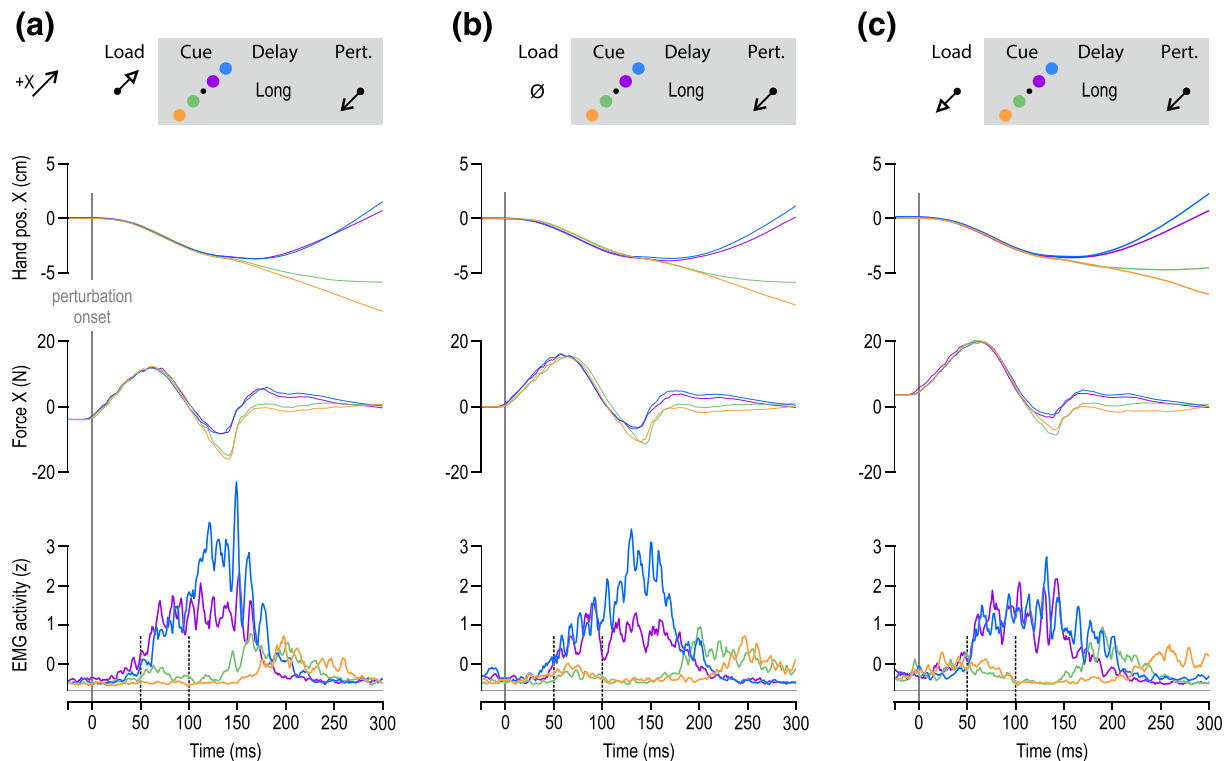
FIGURE 2 Responses from the pectoralis muscle of a single participant in the delayed-reach task. Blue and purple traces represent trials where 'far' and 'near' targets were placed in the +X direction, respectively. These targets require shortening of the pectoralis in order to be reached. Orange and green traces represent trials where 'far' and 'near' targets were placed in the −X direction, respectively. These targets require stretch of the pectoralis in order to be reached. All data in this figure represent median responses across relevant trials that involved a long preparatory delay (750 ms). (a) A slow-rising load was first applied in the +X direction, unloading the pectoralis prior to the haptic perturbation, the onset of which is signified as time zero. (b) As (a), but no load was applied prior to the haptic perturbation. (c) As (a), but the slow-rising load was applied in the −X direction, loading the pectoralis prior to stretch. EMG, electromyography.
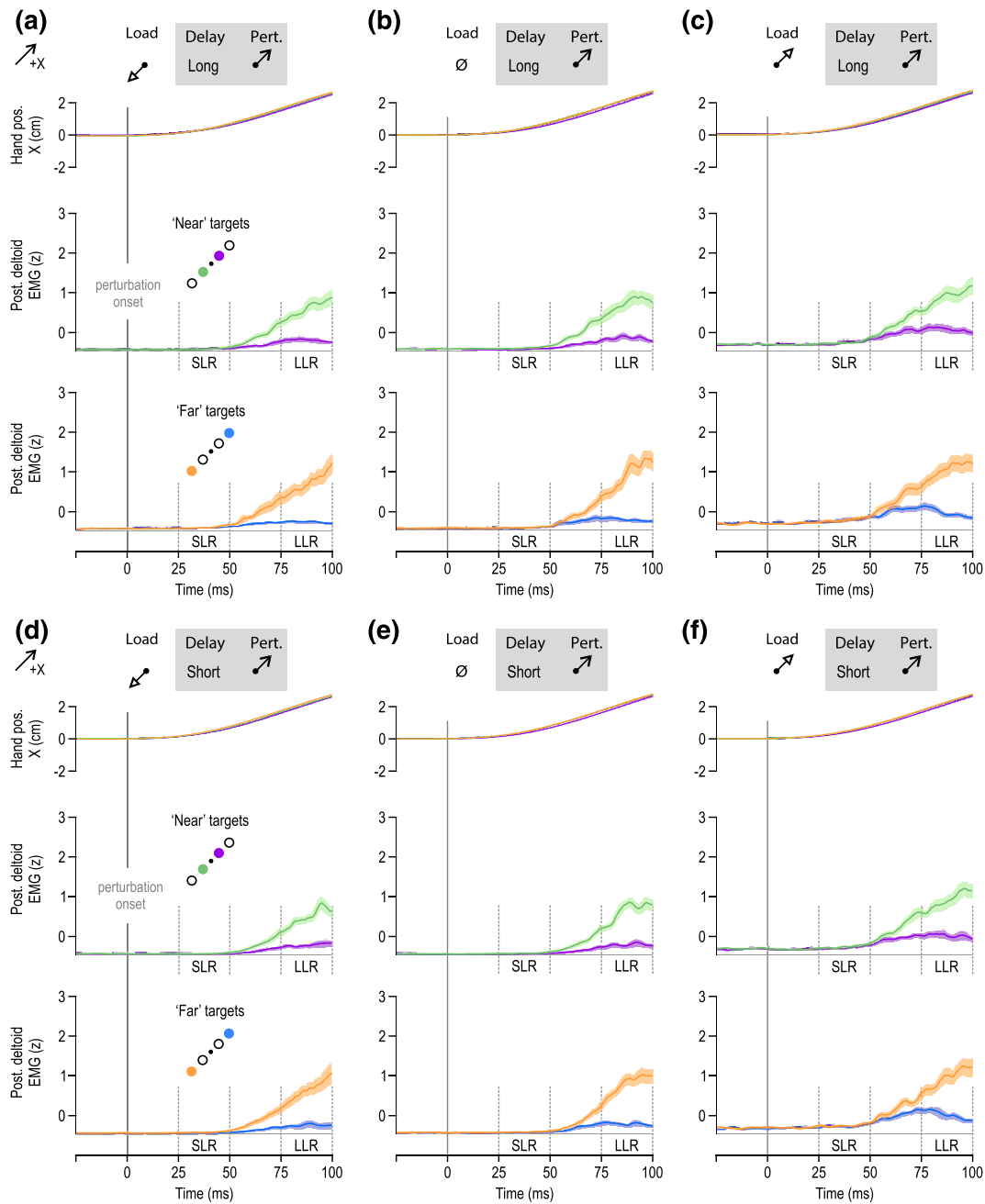
FIGURE 3 Stretch reflex responses in the pectoralis major of the non-dominant limb. Throughout, blue and purple traces represent trials where participants had to reach the 'far' and 'near' targets in the +X direction, respectively. Reaching these targets required shortening of the pectoralis. Orange and green traces represent trials where the participant had to reach the 'far' and 'near' targets in the −X direction, respectively. These trials require stretch of the pectoralis. Throughout, colour shading represents ±1 SEM. (a) The upper panel represents mean hand position across participants ($N = 16$), for all trials where the pectoralis muscle was unloaded before being stretched by the haptic perturbation, following a long preparatory delay (750 ms). The middle row displays mean pectoralis electromyography (EMG) activity across participants for the subset of trials where one or the other 'near' targets were cued for a long delay before pectoralis stretch; the bottom panel represents the equivalent for 'far' targets. (b) As (a), but representing the 'no-load' trials. (c) As (a) but representing trials where the pectoralis was loaded before the stretch perturbation. (d–f) As (a)–(c) but representing trials where the preparatory delay was relatively short (250 ms). LLR, long latency reflex; SLR, short latency reflex.

3.2 | The pre-perturbation epoch

The pre-perturbation epoch (i.e., 25 ms period before perturbation onset) was characterized by significant main effects of load in all three analysed shoulder muscles (i.e., anterior deltoid, posterior deltoid and pectoralis). Specifically, as expected, there was significantly higher pectoralis EMG activity when the muscle was loaded,

FIGURE 4 Stretch reflex responses in the posterior deltoid of the non-dominant limb. Throughout, blue and purple traces represent trials where participants had to reach the 'far' and 'near' targets in the +X direction, respectively. Reaching these targets required stretch of the posterior deltoid. Orange and green traces represent trials where the participant had to reach the 'far' and 'near' targets in the −X direction, respectively. These trials require shortening of the posterior deltoid. Throughout, colour shading represents ±1 SEM. (a) The upper panel represents mean hand position across participants ($N = 16$), for all trials where the posterior deltoid muscle was unloaded before being stretched by the haptic perturbation, following a long preparatory delay (750 ms). The middle row displays mean posterior deltoid electromyography (EMG) activity across participants for the subset of trials where one or the other 'near' targets were cued for a long delay before posterior deltoid stretch; the bottom panel represents the equivalent for 'far' targets. (b) As (a) but representing the 'no-load' trials. (c) As (a) but representing trials where the posterior deltoid was loaded before the stretch perturbation. (d–f) As (a)–(c) but representing trials where the preparatory delay was relatively short (250 ms). LLR, long latency reflex; SLR, short latency reflex.

with the lowest pre-perturbation values observed when the muscle was unloaded ($F_{2,30} = 80.1$, $p < 10^{-5}$, $\eta_p^2 = .84$; Tukey's HSD loaded vs. no load: $p = .0001$; loaded vs. unloaded: $p = .0001$; no load vs. unloaded: $p = .0024$). For the anterior deltoid, there was also a main effect of load on pre-perturbation EMG activity

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$(F_{2,30} = 6.9$, $p = .0034$, $\eta_p^2 = .31)$ with Tukey's HSD test indicating significantly higher values when the muscle was loaded (vs. unloaded: $p = .01$; vs. no load: $p = .007$). Finally, the posterior deltoid also showed a main effect of load on pre-perturbation activity $(F_{2,30} = 36.3$, $p < 10^{-5}$, $\eta_p^2 = .71)$ with Tukey's HSD test indicating significantly higher values when the muscle was loaded (vs. unloaded: $p = .0001$; vs. no load: $p = .0001$).

For the pectoralis muscle alone, there was also a main effect of target direction on the pre-perturbation EMG activity $(F_{1,15} = 10.2$, $p = .006$, $\eta_p^2 = .41)$, with higher values observed when preparing to reach targets in the direction of pectoralis shortening. For the posterior deltoid, there was also a main effect of preparatory delay (long > short; $F_{1,15} = 6.6$, $p = .021$, $\eta_p^2 = .3$) and an interaction effect between delay and target distance, with $F_{1,15} = 5.2$, $p = .04$ and $\eta_p^2 = .26$. However, Tukey's HSD test indicated that the impact of preparatory delay was present regardless of whether the target was 'near' or 'far' (all $p < .031$), but there were no significant differences involving target distance (i.e., short delay 'far' vs. 'near': $p = .9$; long delay 'far' vs. 'near': $p = .094$). Therefore, only in the pectoralis did target parameters affect pre-perturbation EMG activity. That is, there were no other main effects or interaction effects involving target parameters (or preparatory delay) in any of the analysed muscles (all $p > .056$). It would therefore appear that, when preparing to reach with the non-dominant arm, target location impacts the pre-perturbation activity of the pectoralis in a statistically significant manner. Interestingly, target location did not affect pre-perturbation activity of the pectoralis of the dominant arm when performing the same (i.e., mirror-equivalent) delayed-reach task (Torell et al., 2023). As described in the following sections, despite the presence of goal-directed differences in pre-perturbation EMG in the non-dominant limb, equivalent tuning of stretch reflexes in the non-dominant limb was markedly reduced compared with that observed in the dominant limb.

3.3 | The SLR epoch

As mentioned in Section 2, it is well known that automatic gain-scaling due to muscle pre-loading limits the ability to unmask goal-directed modulation of SLR gains, due to the saturation of the goal-directed SLR response (Figures 2–4). Therefore, current analysis of the SLR responses focuses on the 'no-load' and 'unloaded' conditions. That is, the ANOVA design in this case is 2 (preparatory delay) × 2 (load) × 2 (target distance) × 2 (target direction).

We found a consistent main effect of preparatory delay across all three shoulder muscles (Figure 5), with

stronger SLR responses following a long delay (pectoralis: $F_{1,15} = 13.1$, $p = .003$, $\eta_p^2 = .47$; anterior deltoid: $F_{1,15} = 11.0$, $p = .005$, $\eta_p^2 = .42$; posterior deltoid: $F_{1,15} = 12.1$, $p = .003$, $\eta_p^2 = .45$). For the anterior deltoid, there were no other significant main or interaction effects on its SLR responses (all $p > .12$). For the pectoralis and posterior deltoid, there was also a main effect of load on the SLR (pectoralis: $F_{1,15} = 17.6$, $p = .0008$, $\eta_p^2 = .54$; posterior deltoid: $F_{1,15} = 12.4$, $p = .003$, $\eta_p^2 = .45$), with weaker overall responses when the homonymous muscle was unloaded. For both these muscles, there was also a main effect of target direction (pectoralis: $F_{1,15} = 4.9$, $p = .043$, $\eta_p^2 = .25$; posterior deltoid: $F_{1,15} = 12.1$, $p = .003$, $\eta_p^2 = .44$), with stronger SLR responses when preparing to reach a target requiring shortening of the homonymous muscle (Figure 5a,c, respectively). For the posterior deltoid alone, there was also a main effect of target distance $(F_{1,15} = 10.6$, $p = .005$, $\eta_p^2 = .41)$, with significantly higher SLR responses when preparing to reach 'far' versus 'near' targets, although the difference was quite small (difference between means = .0085 z).

To further describe the goal-directed modulation of the SLR, ROC analyses were used. As ANOVA did not show a consistent effect of target distance on SLR responses, the data were collapsed across target distance. Hence, the ROC analyses concentrate on the impact of target direction. The relevant difference signals were created by contrasting the EMG curve observed when the cued targets were in the direction of homonymous muscle stretch versus EMG curves of cued targets were in the direction of muscle shortening. In this way, the ROC curves were used to determine the time point at which the target direction-related signals could be discriminated by an ideal observer. For the unloaded pectoralis (Figure 6a), dog leg fits indicated deviance at 44 ms, for the no-load condition at 46 ms and for the loaded condition at 53 ms. For the unloaded posterior deltoid (Figure 6b), this occurred at 51 ms, for the no-load condition at 44 ms and for the loaded condition at 54 ms. The onset times were also calculated for each participant individually (small red circles in Figure 6a,b). The time point at which the ROC was above .75 was also identified and indicated as red vertical lines. For the unloaded pectoralis (Figure 6a), this occurred at 63 ms, for the no-load condition at 68 ms and for the loaded condition at 66 ms. For the unloaded posterior deltoid (Figure 6b), this occurred at 69 ms, for the no-load condition at 70 ms and for the loaded condition at 66 ms.

Compared with the previously performed ROCs in Torell et al. (2023) pertaining to the dominant arm, the modulation onset for unloaded pectoralis was 25 ms slower in the non-dominant arm; similarly, for the no-load condition, the modulation onset occurred 23 ms
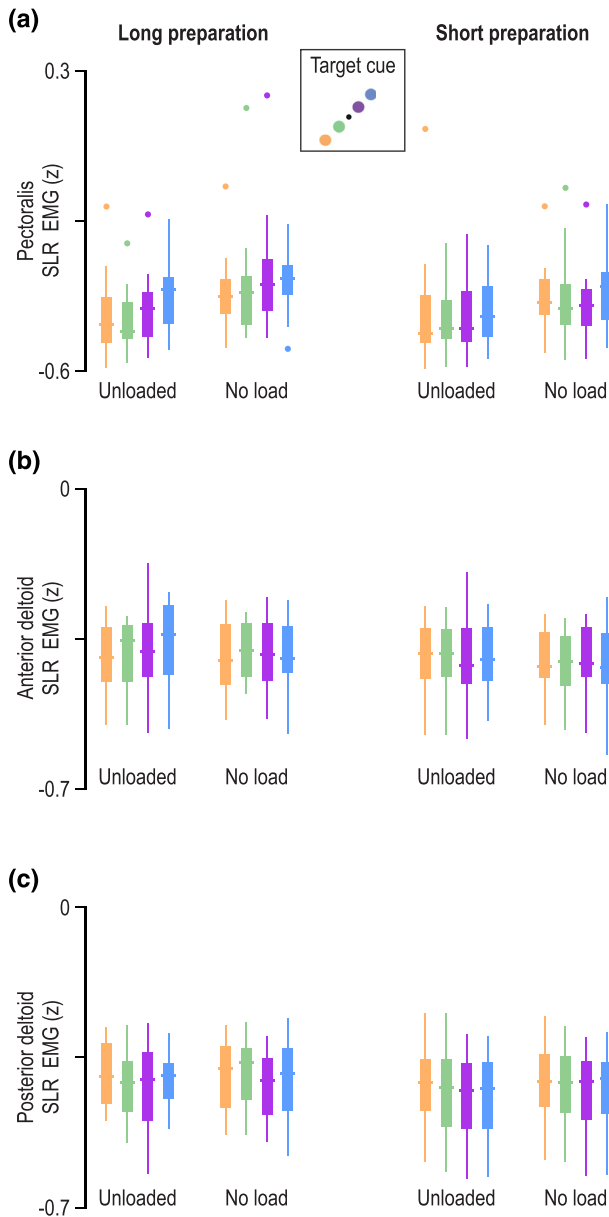
FIGURE 5 Lack of a consistent goal-directed modulation of short latency reflex (SLR) gains in the non-dominant limb. (a) Colour coding as in previous figures. Each boxplot was created using the averaged pectoralis SLR electromyography (EMG) activity (z) of each participant ($N = 16$). Specifically, as in all boxplots of the current paper, thick vertical lines represent the 25th to 75th percentile range of the relevant averaged values, and the thin lines represent the remaining distribution of data except for outliers (thin dots), defined as data points outside ~2.7 standard deviations from the mean. The panel on the left represents SLR responses when the preparatory delay was long, and the panel on the right represents SLR responses when the preparatory delay was short. (b) As (a) but representing the anterior deltoid muscle. There was no goal-directed modulation of anterior deltoid SLR. (c) As (a) but representing the posterior deltoid.

slower in the non-dominant arm. For the loaded pectoralis, the modulation onset occurred 19 ms later in the non-dominant arm. For the posterior deltoid, the modulation onset for the unloaded muscle occurred 23 ms slower. Similarly, for the no-load condition, it was 3 ms slower and for the loaded posterior deltoid, the onset occurred 4 ms later. In other words, the modulation differences were the strongest for the unloaded muscle.

The time point at which the ROC was above .75 was also compared. For the unloaded pectoralis, the point of significant discrimination was delayed by 18 ms when the non-dominant arm was used. Similarly, for the no-load condition, significant discrimination could be achieved 8 ms faster using the dominant arm. For the unloaded pectoralis, the difference was 9 ms, once again in favour of the dominant arm. For the unloaded posterior deltoid, significant discrimination could be achieved 17 ms faster for the dominant arm compared with the non-dominant arm. Similarly, for the no-load condition and the unloaded posterior deltoid, it was 9 and 3 ms, respectively. Once again, the earliest goal-directed modulation in stretch reflex responses was evident for the unloaded muscle.

3.4 | The LLR epoch

To examine LLR responses of muscles in the non-dominant limb, we used the complete ANOVA design of 2 (preparatory delay) × 3 (load) × 2 (target distance) × 2 (target direction). There was a main effect of load on the LLR responses of all three analysed muscles (Figure 7; pectoralis: $F_{2,30} = 12.7$, $p = .0001$, $\eta_p^2 = .46$; anterior deltoid: $F_{2,30} = 14.7$, $p = .00004$, $\eta_p^2 = .50$; posterior deltoid: $F_{2,30} = 22.2$, $p < 10^{-5}$, $\eta_p^2 = .60$). Tukey's HSD test showed that LLR EMG activity was significantly higher when the pectoralis was loaded (vs. unloaded: $p = .0004$; vs. no load: $p = .0006$), when the anterior deltoid was loaded (vs. unloaded: $p = .002$; vs. no load: $p = .0002$) and when the posterior deltoid was loaded (vs. unloaded: $p = .0001$; vs. no load: $p = .0006$). There was also a main effect of target direction on the LLR responses of all three muscles, with higher gains evident when preparing to reach targets associated with homonymous muscle shortening (pectoralis: $F_{1,15} = 60.0$, $p < 10^{-5}$, $\eta_p^2 = .80$; anterior deltoid: $F_{1,15} = 22.6$, $p = .0003$, $\eta_p^2 = .60$; posterior deltoid: $F_{1,15} = 74.0$, $p < 10^{-5}$, $\eta_p^2 = .83$). For the anterior deltoid, there was also a significant main effect of preparatory delay ($F_{1,15} = 8.1$, $p = .012$, $\eta_p^2 = .35$), with stronger responses following a long preparatory delay. There was also a main effect of target distance on anterior deltoid LLR ($F_{1,15} = 6.3$, $p = .024$, $\eta_p^2 = .29$), with stronger

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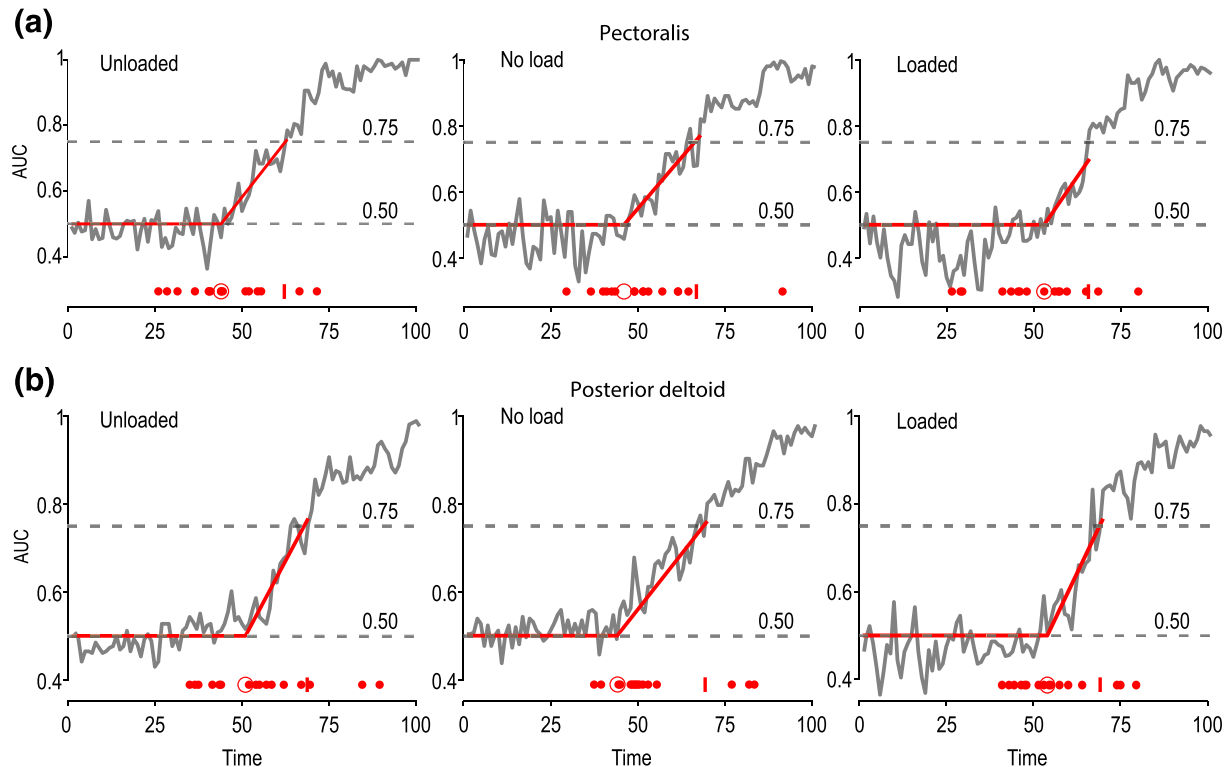
FIGURE 6 The time onset of short latency reflex (SLR) modulation. (a) The grey curve in each panel represents the area under the receiver operating characteristic (ROC), pertaining to pectoralis SLR modulation as a function of target direction, after experiencing one of the three load conditions ('unloaded', 'no load' or 'loaded') and a long preparatory delay (see Sections 2 and 3 for more details). Specifically, vertical axes represent the probability that an ideal observer could discriminate between the electromyography (EMG) difference curves. Each solid red line represents a dog leg fit that was applied to determine the onset of significant SLR modulation as a function of target direction (see also larger red circle at the bottom of each panel). The small red vertical line at the bottom of each panel represents the time point when the ROC area remained >.75 for five consecutive time points (i.e., five consecutive milliseconds). The smaller red dots represent the ROC result for each individual participant. (b) As (a) but representing the posterior deltoid. AUC, area under the curve.

responses for 'far' versus 'near' targets, but no such main effect was evident for the pectoralis or posterior deltoid ($p = .43$ and $p = .13$, respectively). In short, across all analysed muscles, there were consistent main effects of load and target direction on LLR responses.

In addition to the main effects, there were also significant two-factor interaction effects on the LLR responses. The ANOVA indicated a significant interaction effect between delay and target direction for both the pectoralis and anterior deltoid (pectoralis: $F_{1,15} = 27.5$, $p = .00001$, $\eta_p^2 = .65$; anterior deltoid: $F_{1,15} = 20.7$, $p = .0004$, $\eta_p^2 = .58$). For both these muscles, Tukey's HSD test showed that the impact of preparatory delay on LLR responses (long- > short) was evident only when preparing to reach targets requiring shortening of the homonymous muscle (i.e., blue and purple in Figure 7a,b; $p < .008$). In addition, there was a significant interaction effect between target distance and target direction on pectoralis and posterior deltoid LLR responses (pectoralis: $F_{1,15} = 5.4$, $p = .035$, $\eta_p^2 = .26$; posterior deltoid: $F_{1,15} = 21.2$, $p = .0003$, $\eta_p^2 = .59$). Tukey's HSD test showed that, for the

pectoralis, there was some impact of distance ('far' > 'near') only when comparing targets of a different direction ($p > .23$ for same-direction comparisons). In addition, for the posterior deltoid, Tukey's HSD test indicated a significant impact of target distance on LLR responses ('far' > 'near') when preparing to reach targets associated with homonymous muscle shortening ($p = .001$; orange vs. green in Figure 7c).

For the pectoralis muscle, there was an additional interaction effect between preparatory delay and load ($F_{2,30} = 4.0$, $p = .028$, $\eta_p^2 = .21$) with Tukey's HSD test showing that the impact of delay on pectoralis LLR (long- > short) was evident when the pectoralis was unloaded ($p = .012$). Last, there was an interaction effect between load and target direction on anterior deltoid LLR ($F_{2,30} = 7.9$, $p = .002$, $\eta_p^2 = .34$). Tukey's HSD test showed that the majority of the two-factor interactions were significant, except for comparisons of targets placed in the direction requiring muscle stretch (all $p > .10$). Nevertheless, despite the various interaction effects, it is rather clear that LLR gains in the non-dominant upper limb
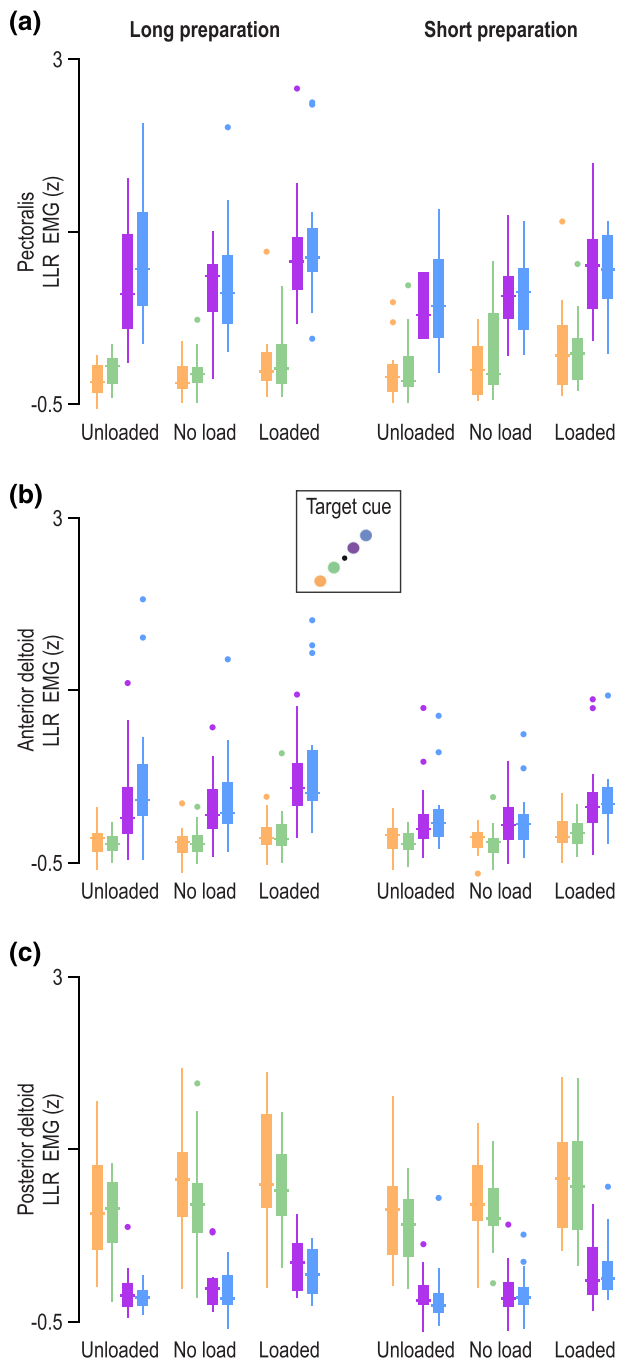
FIGURE 7 Goal-directed modulation of long latency reflex (LLR) gains in the non-dominant limb. (a) Each boxplot was created using the averaged pectoralis LLR electromyography (EMG) activity (z) of each participant ($N = 16$). Colour coding as in Figure 5 (see also schematics in (b)). The panel on the left represents LLR responses when the preparatory delay was long, and the panel on the right represents LLR responses when the preparatory delay was short. Analyses of variance indicated a significant impact of target direction on pectoralis LLR gains. (b) As (a) but representing the anterior deltoid muscle. Similar LLR modulation patterns were observed as for the pectoralis. (c) As (a) but representing the posterior deltoid. Equivalent LLR modulation patterns were observed as for the pectoralis.

were primarily influenced by target direction, as can be appreciated by visually inspecting Figure 7.

3.5 | Reflex tuning in the dominant versus non-dominant upper limbs

To compare goal-directed tuning of stretch reflex responses in the dominant versus non-dominant arms, we use the data recorded for the purposes of this study and additional data published recently (Torell et al., 2023), where a separate group of participants performed the equivalent experiment using their right dominant arm. Because target direction was the primary factor shaping reflex gains in both the dominant and non-dominant arms, the following analyses use data that were collapsed across target distances (i.e., green/orange were combined, as were blue/purple; e.g., Figure 7), so that goal only represents target direction in this case. Moreover, in order to simplify analyses and produce a measure that is more directly representative of goal-dependent tuning, the responses observed when preparing to stretch the homonymous muscle (i.e., preparing to reach a target associated with muscle lengthening) were subtracted from the responses observed when preparing to shorten the homonymous muscle (see schematics in Figures 8 and 9). As the anterior deltoid of the non-dominant arm showed no goal-directed modulation of SLR gains (Figure 5b), the following analyses of shoulder muscles are limited to the posterior deltoid and pectoralis.

With regard to the unloaded pectoralis major, an independent t-test with z-normalized data indicated stronger goal-directed tuning of SLR gains in the dominant arm following a long preparatory delay ($t_{28} = 2.4$, $p = .022$), with no corresponding difference in pre-perturbation activity ($t_{28} = .0009$, $p = .99$; Figure 8a, leftmost bars). The difference in pectoralis SLR between the dominant and non-dominant limbs failed to reach significance in the no-load condition following a long delay ($t_{28} = 1.87$, $p = .07$). However, a single-sample t-test showed that pectoralis SLR responses from the dominant limb (cyan) were significantly different from zero ($t_{13} = 2.93$, $p = .012$), confirming the presence of a goal-directed tuning in this case, whereas this was not so for SLR responses from the non-dominant limb ($t_{15} = 1.68$, $p = .1$). There were no differences in SLR tuning when the pectoralis muscle was loaded ($t_{28} = 1.37$, $p = .18$), nor under any load condition when the preparatory delay was short (right panel in Figure 8a; brown vs. cyan unloaded: $p = .09$; no load: $p = .3$; loaded: $p = .13$). Note the gradual decrease in SLR gain of the dominant pectoralis from left to right in Figure 8a (cyan bars),
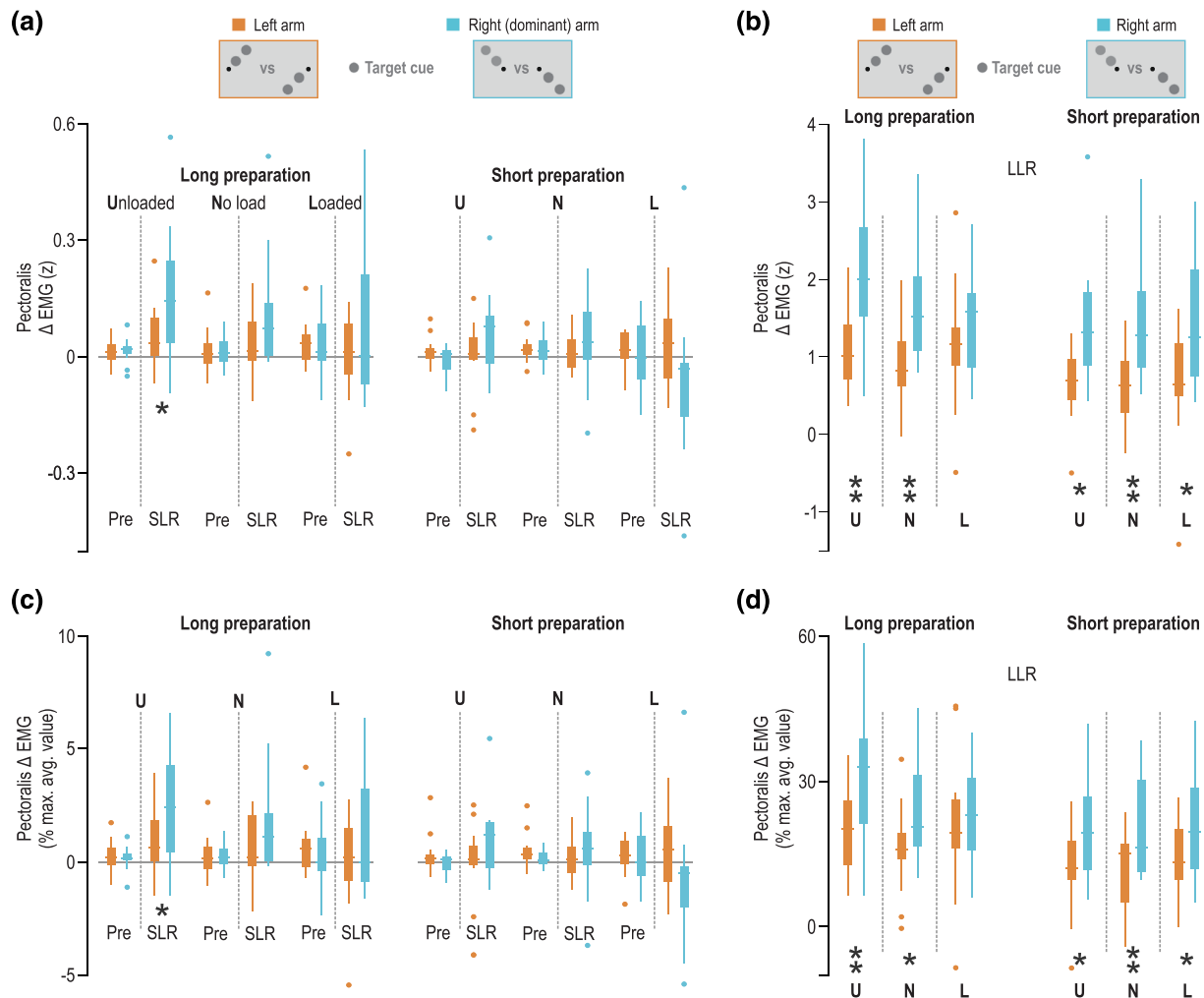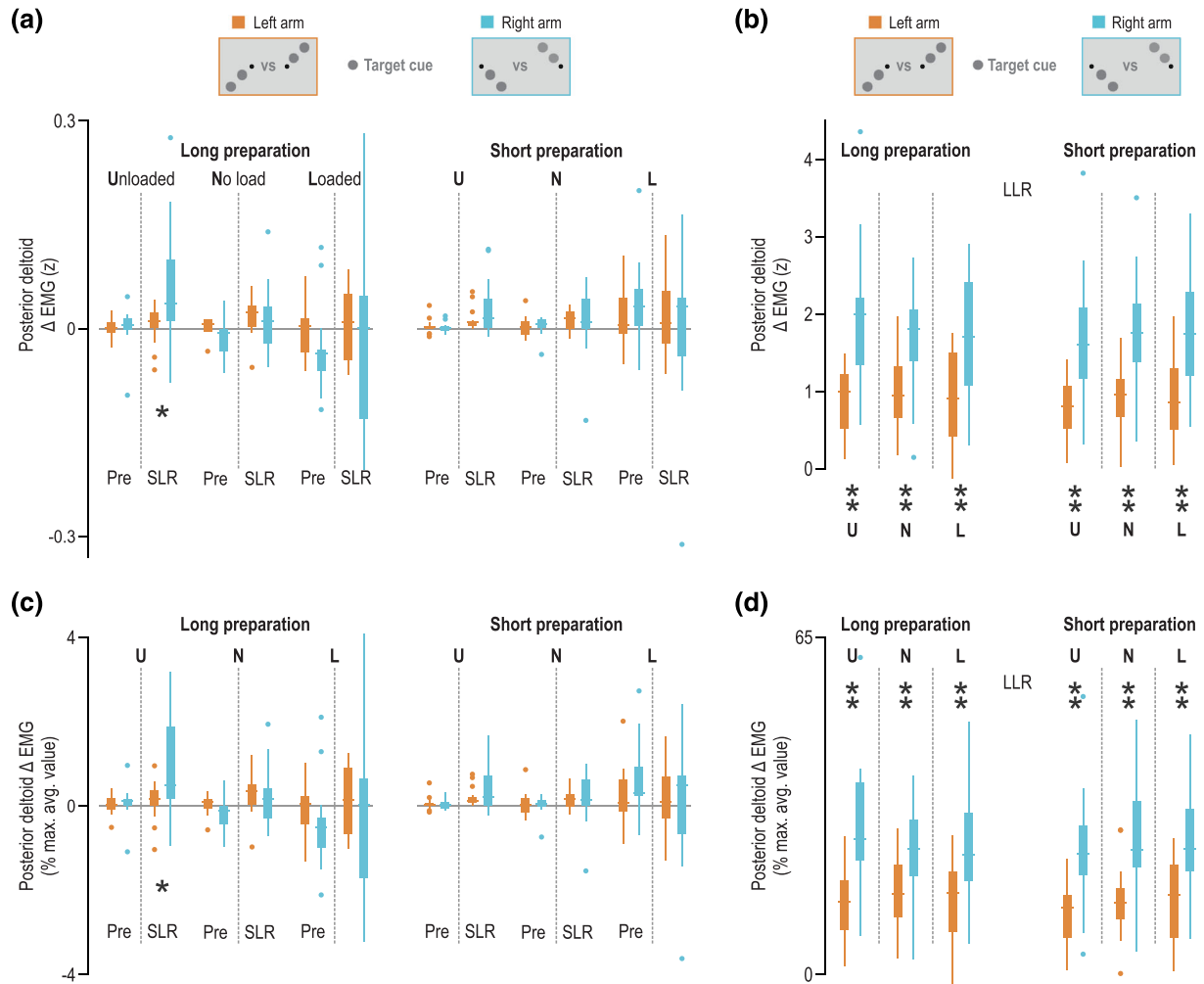
FIGURE 8 Goal-directed tuning of pectoralis stretch reflexes in the dominant versus non-dominant limbs. (a) Boxplots in brown represent goal-directed change in pectoralis electromyography (EMG) activity (z) of the non-dominant arm, across participants (N = 16) during the pre-perturbation and short latency reflex (SLR) epochs. The relevant averaged values for each individual muscle were generated by subtracting EMG activity observed in trials where participants prepared to stretch the homonymous muscle from the activity observed when preparing muscle shortening (i.e., activity in trials where reaching the cued target required shortening of the homonymous muscle; see also schematics). Cyan bars represent the corresponding EMG data of a group of participants (N = 14) who performed the equivalent delayed-reach task using their dominant/right limb. Throughout, 'Pre' represents the pre-perturbation epoch, single stars represent a significant difference following an independent t-test (brown vs. cyan) at alpha = .05 and double stars indicate statistical significance at alpha = .01. (b) As (a) but representing the long latency reflex (LLR) response. (c, d) As (a) and (b) but, here, EMG activity from each individual muscle was normalized as a proportion (%) of the maximal mean value across trials (see Section 2 for more details).

highlighting earlier findings that longer preparation and unloading (i.e., 'assistive' loading) promote the goal-directed modulation of stretch reflex gains.

Figure 8b displays the goal-directed LLR responses of the pectoralis in the dominant and non-dominant limbs. When the preparatory delay was long, there was significantly stronger goal-directed tuning of LLR gains in the dominant arm when the muscle was unloaded ($t_{28} = 3.78$, $p = .0008$) and when there was no load ($t_{28} = 3.31$, $p = .003$). Interestingly, there was no corresponding difference in LLR tuning when the pectoralis of the dominant and non-dominant arms was loaded ($t_{28} = 1.38$, $p = .18$). In contrast, when the preparatory delay was short, pectoralis LLR gains were significantly higher in the dominant arm under all load conditions (unloaded: $t_{28} = 2.66$, $p = .013$; no load: $t_{28} = 3.43$, $p = .002$; loaded: $t_{28} = 2.64$, $p = .013$).

Equivalent significant differences were obtained for the SLR and LLR when the %-normalized pectoralis activity was analysed (Figure 8c,d). Specifically, for the unloaded pectoralis, a t-test indicated stronger goal-directed tuning of SLR gains in the dominant arm following a long preparatory delay ($t_{28} = 2.2$, $p = .035$), with no corresponding difference in pre-perturbation activity

FIGURE 9 Goal-directed tuning of posterior deltoid stretch reflexes in the dominant versus non-dominant limbs. (a) Boxplots in brown represent goal-directed change in posterior deltoid electromyography (EMG) activity (z) of the non-dominant arm, across participants ($N = 16$). The relevant values were generated as per Figure 8a,b (see also schematics) and pertain to the pre-perturbation and short latency reflex (SLR) epochs. Cyan bars represent the corresponding EMG data of a separate group of participants ($N = 14$) who performed the equivalent delayed-reach task using their dominant/right limb. Throughout, 'Pre' represents the pre-perturbation epoch, single stars represent a significant difference following an independent t-test (brown vs. cyan) at alpha = .05 and double stars indicate statistical significance at alpha = .01. (b) As (a) but representing the long latency reflex (LLR) response. (c, d) As (a) and (b) but, here, EMG activity from each individual muscle was normalized as a proportion (%) of the maximal mean value across trials.

($t_{28} = -.5$, $p = .62$; Figure 8c, leftmost bars). When the preparatory delay was long, there was significantly stronger goal-directed tuning of LLR gains in the dominant arm when the muscle was unloaded ($t_{28} = 2.89$, $p = .007$) and when there was no load ($t_{28} = 2.47$, $p = .02$). When the preparatory delay was short, pectoralis LLR gains were significantly higher in the dominant arm under all load conditions (unloaded: $t_{28} = 2.37$, $p = .025$; no load: $t_{28} = 2.81$, $p = .009$; loaded: $t_{28} = 2.07$, $p = .047$).

Similar reflex tuning patterns are evident for the posterior deltoid (Figure 9). With regard to the unloaded muscle, we found stronger goal-directed tuning of SLR gains in the dominant arm following a long preparatory delay ($t_{28} = 2.37$, $p = .025$), again with no corresponding

difference in pre-perturbation activity ($t_{28} = -.017$, $p = .97$; Figure 9a, leftmost bars). There was no difference in posterior deltoid tuning between the dominant and non-dominant limbs in the no-load condition ($t_{28} = -.41$, $p = .67$) or the loaded condition ($t_{28} = -.98$, $p = .37$), following a long delay. When the preparatory delay was short, there were no differences in SLR tuning under any load condition (right panel in Figure 9a; unloaded: $p = .14$; no load: $p = .86$; loaded: $p = .68$). Figure 9b displays the goal-directed LLR responses of the posterior deltoid. Regardless of preparatory delay duration or load condition, goal-directed tuning of posterior deltoid LLR was stronger in the dominant arm (from left to right in Figure 8d: $t_{28} = 3.99$, $p = .0004$; $t_{28} = 3.02$,

$p = .005$; $t_{28} = 2.98$, $p = .006$; $t_{28} = 3.58$, $p = .0013$; $t_{28} = 3.76$, $p = .0008$; $t_{28} = 3.66$, $p = .001$).

Equivalent significant differences were obtained for the SLR and LLR when the %-normalized posterior activity was analysed (Figure 9c,d). Specifically, for the unloaded posterior deltoid, there was stronger goal-directed tuning of SLR gains in the dominant arm following a long preparatory delay ($t_{28} = 2.4$, $p = .024$) and no corresponding difference in pre-perturbation activity ($t_{28} = .034$, $p = .74$; Figure 9c, leftmost bars). Regardless of preparatory delay duration or load condition, goal-directed tuning of posterior deltoid LLR was stronger in the dominant arm (from left to right in Figure 9d: $t_{28} = 3.82$, $p = .0007$; $t_{28} = 2.79$, $p = .009$; $t_{28} = 2.8$,

$p = .008$; $t_{28} = 3.48$, $p = .0017$; $t_{28} = 3.42$, $p = .0019$; $t_{28} = 3.5$, $p = .0016$).

Overall, regardless of which of the two normalization procedures was used, equivalent statistical results were obtained for shoulder muscles. Our results demonstrate a markedly weaker goal-directed tuning of stretch reflexes in the non-dominant limb, and this laterality in motor behaviour was particularly robust in the LLR epoch. To confirm previous results that pointed to reduced goal-directed tuning of stretch reflexes in elbow muscles compared with the shoulder muscles in our paradigm, we also performed analyses of the recorded brachioradialis, biceps, triceps longus and lateralis LLR. As indicated in Figure 10, goal-directed difference in LLR EMG of elbow
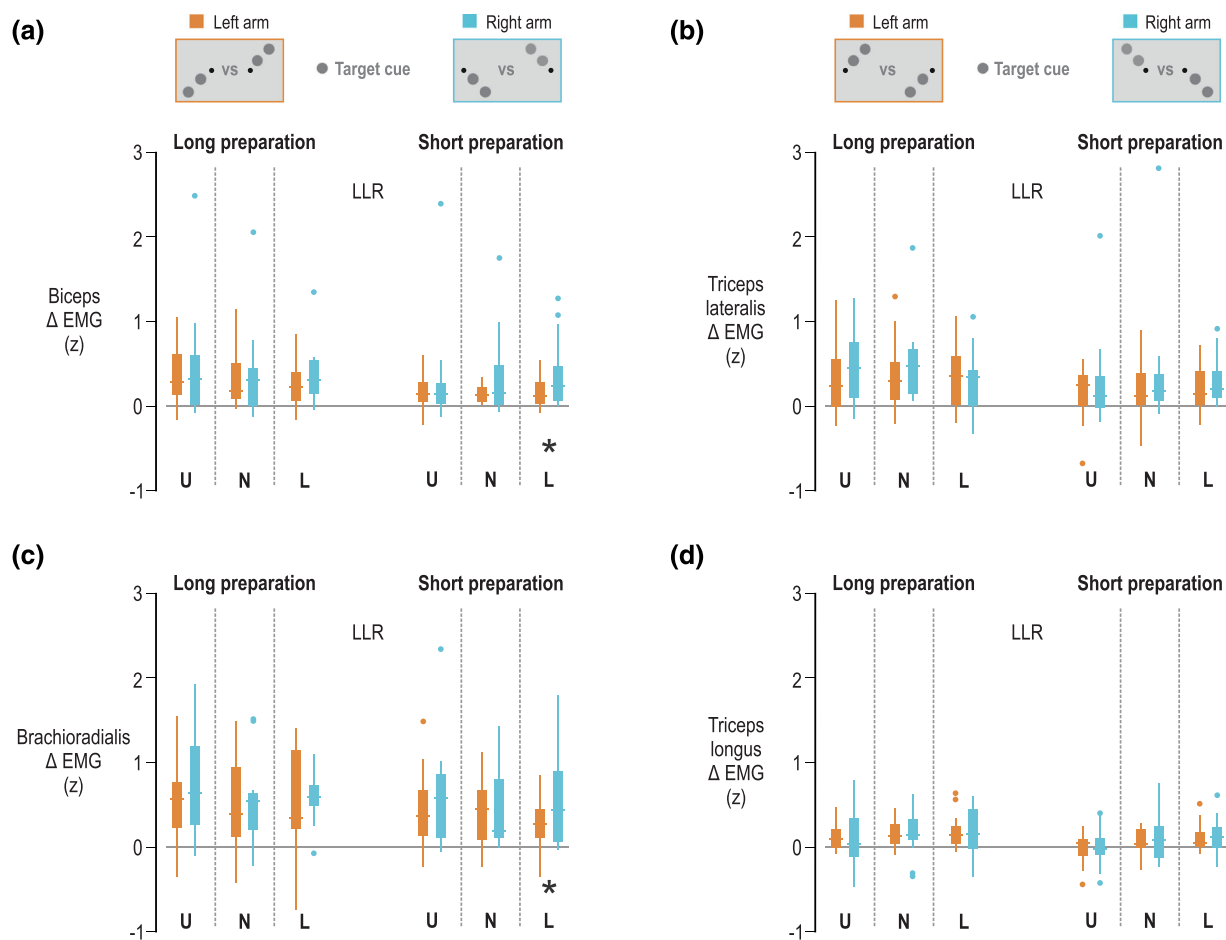
FIGURE 10 Reduced goal-directed tuning of stretch reflexes at the level of the elbow. (a) Boxplots in brown represent goal-directed change in biceps electromyography (EMG) activity (z) of the non-dominant arm, across participants ($N = 16$). The relevant values were generated as per Figure 8a,b (see also schematics). Cyan bars represent the corresponding EMG data of a separate group of participants ($N = 14$) who performed the equivalent delayed-reach task using their dominant/right limb. Throughout, the data pertain to the long latency reflex (LLR) epoch, single stars represent a significant difference following an independent t-test (brown vs. cyan) at alpha = .05, 'L' represents (pre-)loaded muscle, 'N' refers to no load and 'U' refers to unloaded muscle, as per previous figures. As expected for this particular delayed-reach task, goal-directed tuning of stretch reflexes from muscles at the level of the elbow were reduced compared with those observed from shoulder muscles (see, e.g., Figure 9b; equivalent scales). (b–d) As (a) but representing the triceps lateralis, brachioradialis and triceps longus muscles, respectively.

muscles was generally <.5 z for both arms, whereas the goal-directed tuning of, for example, the posterior deltoid of the non-dominant arm was around 1 z in size and ~2 z in the dominant arm (i.e., Figure 10 vs. Figure 9b). Moreover, independent t-tests indicated a significant difference in goal-directed tuning of LLR gains (dominant > non-dominant) only in two instances at the elbow, namely, in the case of the loaded brachioradialis ($t_{28} = 2.3$, $p = .029$) and the loaded biceps ($t_{28} = 2.37$, $p = .025$) when the delay was short (but note overall higher values for long delays). Although there seems to be a general trend for stronger goal-directed tuning of elbow LLR of the dominant arm, paralleling the robust difference in LLR tuning at the shoulder, all other comparisons reflected in Figure 10 were not statistically significant (all other $p > .07$ for the biceps; all other $p > .19$ for the brachioradialis; all $p > .14$ for the triceps lateralis; all $p > .6$ for the triceps longus).

4 | DISCUSSION

In this study, we investigate the neural mechanisms that underlie the preparation for goal-directed movements in the non-dominant arm. The stretch reflexes in the non-dominant arm were examined using the same design used for the dominant arm (Torell et al., 2023). Participants were presented with four targets varying in both direction and distance, and three background loads. After target presentation, a rapid perturbation was applied to the arm at one of two delays (short or long) to probe the preparatory tuning of stretch reflexes. We found small goal-directed differences in the background (pre-perturbation) muscle activity but only minor differences in the short latency stretch reflex as a function of target location. The only consistent effect at the short latency was that of preparatory time, where we found stronger responses for the longer delay times. At the long latency interval, we found consistent effects of both load and target direction on the stretch reflex responses. Finally, we compared the goal-directed stretch reflex tuning found in the non-dominant arm with that previously seen in the dominant arm. The results clearly show much stronger goal-directed modulation of stretch reflex responses in the dominant arm, both in the SLR and LLR intervals.

One possible explanation of the SLR and LLR amplitude differences could be differences in the alpha motor neuron density projecting to the dominant and non-dominant arms. However, the amount of spinal motor neurons does not differ significantly between arms (Li et al., 2015). In addition, intramuscular EMG recordings have shown that right-handed individuals have no dominance-related differences in single motor unit action

potentials (Nelson et al., 2003). On the other hand, genetics or long-term preferential use of the dominant arm seem to affect muscle fibre composition. The proportion of Type I muscle fibres is significantly higher in the dominant arm of right-handed individuals (Fugl-Meyer et al., 1982). Studies using surface EMG have also indicated asymmetric muscle composition related to dominance (Merletti et al., 1994; Williams et al., 2002), which may in turn lead to differences in motor unit function (Adam et al., 1998). While different factors and mechanisms likely affect the laterality of motor performance, including endocrine effects on spinal neuronal elements (Bakalkin, 2022; Lukoyanov et al., 2021), our results are largely based on within-muscle metrics of goal-directed tuning (e.g., see Figures 8 and 9). As elaborated below, we propose that subtle differences in strategies of feedforward control between the dominant and non-dominant arms, particularly the differential control of gamma motor neurons, facilitated the observed asymmetries in SLR and LLR response amplitudes.

One potential limitation of the current study is that a different group of participants was examined compared with our previous study that documented reflex tuning in the dominant upper limb (Torell et al., 2023). Although comparing the stretch reflex modulation in the left and right limbs of the same participants would likely provide stronger statistical power, the SLR and LLR differences between the dominant and non-dominant limbs in our study are nevertheless clear across all investigated muscles. Moreover, relevant analyses were conducted using normalized data, including normalization based on the maximal activation values observed in each individual muscle (Figures 8 and 9).

Although there was evidence for a goal-directed modulation of reflex responses in the non-dominant arm, this tuning was clearly weaker than that observed in the dominant arm. However, we again found that the goal-directed modulation, particularly of the LLR, was more pronounced when sufficient preparatory time was allowed. Despite the similarity in the response patterns across both the dominant and non-dominant limbs, a comparison shows much greater goal-directed tuning of the reflex gains in the dominant arm prior to reaching. This effect is particularly clear in the LLR epoch (Figures 8b,d and 9b,d) where virtually every comparison showed stronger goal-directed responses in the dominant arm. However, we also observed stronger goal-directed tuning of SLR gains following a longer preparatory delay (Figures 8a,c and 9a,c). The effect of preparatory delay on the goal-directed tuning of stretch reflex gains suggests that motor planning is not only composed of setting up the appropriate descending drive to the extrafusal muscles through alpha motor neuron control but also

tuning the gamma drive independently to provide goal-appropriate feedback. As goal- and delay-directed modulation is evident for both SLR and LLR gains, this suggests a critical role for gamma motor neurons in movement preparation. Such changes in feedback gains take time to develop even for simple reaching movements, where a 250-ms delay shows much less modulation than 750 ms. A similar temporal evolution of LLR gains according to motor planning was shown in the random dot paradigm, where stronger motion coherence produced responses more appropriate for the subsequent movement (Selen et al., 2012).

The difference in goal-directed modulation of reflex responses between the dominant arm and non-dominant arm was largest in the unloaded and no-load conditions when the delay was long (although similar effects are visible in the loaded condition; Figure 8a,c). We have suggested that the strongest goal-directed modulation occurs when the muscle is unloaded because antagonist loading is accompanied by top-down reciprocal inhibition of the lower motor neurons of the muscle, including gamma motor neurons (Dimitriou, 2014). We have hypothesized that the stronger goal-directed modulation develops as the independent goal-directed control of dynamic gamma motor neurons occurs on top of this blanket reciprocal inhibition of lower motor neurons that accompanies muscle unloading (Torell et al., 2023). More specifically, we suggest that preparatory activity before a planned voluntary movement is involved in setting this goal-dependent tuning of muscle spindles just prior to a movement (Papaioannou & Dimitriou, 2021). This effect is dampened by directly loading the muscle as gain-scaling dominates the overall SLR responses, limiting the ability to detect goal-directed tuning (Torell et al., 2023). This is different to the historical view that preparatory activity represents a sub-threshold version of movement-related cortical activity (Tanji & Evarts, 1976). With such a hypothesis, we might be concerned that the no-load or even the unloaded conditions might exhibit different sub-threshold activity of the motor neuron pools that could affect the reflex gains (Bedingham & Tatton, 1984; Matthews, 1996; Pruszynski et al., 2009). However, more recent work has contradicted the idea of sub-threshold preparation, showing instead that preparatory activity sets an initial dynamical state that promotes execution of the planned movement (Churchland et al., 2010).

While preparation lowers reaction time (Rosenbaum, 1980) and benefits movement quality (Ghez et al., 1997), it has been shown that preparation is mechanistically independent from movement initiation (Haith et al., 2016). Such studies motivated the possibility that preparatory activity might reflect the control of proprioceptive sensory feedback, by setting the appropriate goal-directed modulation of the fusimotor system. This possibility was directly tested using microneurography, showing that preparation for moving to a visual target sets changes in spindle stretch sensitivity (Papaioannou & Dimitriou, 2021). But this goal-directed effect takes time to fully develop, and interestingly, spindle firing during preparation predicts time to peak velocity but not reaction time. A very recent study has shown selective ramping up of small motor units in the anterior deltoid muscle during movement preparation, and this activity correlated with reaction time, that is, movement onset (Rungta & Murthy, 2023). Taken together, the above suggest that different mechanisms may be involved in delayed reach, perhaps involving independent controllers (e.g., alpha vs. gamma motor neuron control), with spindle preparatory tuning exerting most of its impact by affecting reflex muscle stiffness during movement, rather than impacting movement initiation and reaction time per se. To assess whether spindle preparatory tuning could affect stretch reflexes, goal-directed modulation was confirmed using a delayed-reach task (Papaioannou & Dimitriou, 2021; Torell et al., 2023). Here, we use an equivalent experimental design to investigate differences in the goal-directed modulation of stretch reflexes across the dominant and non-dominant arms. While we cannot directly confirm that these differences arise due to laterality of fusimotor control across the two arms, this does provide a strong prediction that can be directly tested in future studies.

The dominant arm exhibited stronger goal-directed modulation of stretch reflexes, suggesting that the dominant arm is better at anticipating and controlling reflex muscle stiffness according to the movement goal. Therefore, the dominance differences seen during voluntary movement, such as better fine motor skills (Annett et al., 1979; Shen & Franz, 2005), are also visible in feedback control. Previous research has suggested that the non-dominant side may rely more heavily on proprioceptive feedback (Goble & Brown, 2008b). This fits with the theory that the two hands play different roles in motor control (Bagesteiro & Sainburg, 2003; Sainburg, 2005, 2014; Sainburg & Kalakanis, 2000), with the non-dominant hand controlling position and the dominant hand controlling trajectory. The current theory of motor lateralization is heavily based on findings in individuals with unilateral brain damage (Schaefer et al., 2009, 2012). The theory suggests that right-handed individuals have a dominant (left) hemisphere that accounts for predictive, feedforward control and movement planning, while the non-dominant hemisphere accounts for feedback-mediated error correction. This in turn implies that the non-dominant hand is under impedance control while the dominant hand is under trajectory control through internal predictive models.

The central nervous system (CNS) has the capacity to selectively control muscle spindle sensitivity, an ability that has also been shown in completely relaxed subjects (Ribot-Ciscar et al., 2000). In this way, both hemispheres may contribute significantly to the control of goal-directed movements, where the ipsilateral hemisphere is inhibited using a signalling pathway mediated via the spinal cord (Chen et al., 1997; Fisk & Goodale, 1988; Haaland & Harrington, 1989; Winstein & Pohl, 1995). Transcranial magnetic stimulation has shown that dominance is associated with asymmetrical excitability of the corticospinal system (De Gennaro et al., 2004). De Gennaro et al. found that the dominant hemisphere had lower thresholds in left-handed participants and larger amplitudes of motor evoked potential (MEP) in right-handed participants. Conflicting findings have been presented where MEP was found to be unrelated to arm dominance and instead dependent on the length of the upper extremity (Livingston et al., 2010).

Here, we find differences in the laterality of goal-directed modulation of stretch reflexes in our delayed-reach task. Specifically, we find higher modulation of both SLR and LLR gains according to the future movement goal in the dominant arm. In contrast, there have been limited differences in laterality seen in postural tasks (Maurus et al., 2021; Walker & Perreault, 2015). Walker and Perreault (2015) found little evidence for modulation in reflex sensitivity according to arm dominance across the whole population across the age groups. In a similar postural study, Maurus et al. (2021) examined the reflex sensitivity and directionality between the dominant and non-dominant limbs. They found no evidence for differences in the pattern of reflexes between the two limbs and little difference in the magnitude of the responses. Although this study (Maurus et al., 2021) predicted that the non-dominant limb would exhibit stretch reflexes aligned with single joint motion due to a possible reliance on impedance control, it has long been known that the control of limb impedance requires impedance to be coordinated across all joints to maintain system stability (Franklin et al., 2007; Franklin & Milner, 2003; McIntyre et al., 1995) and, therefore, likely also requires accurate internal models of limb dynamics (Franklin et al., 2008; Tee et al., 2010). We therefore argue that a difference between impedance control and internal model control would be unlikely to show directionality differences in this postural task (Maurus et al., 2021).

Nevertheless, both previous studies showed limited differences in the laterality of stretch reflexes, in contrast to our results, which likely reflect the major differences in the task design. First, both postural task studies pre-load the limbs and muscles limiting the modulation of stretch reflexes (Dimitriou, 2018; Torell et al., 2023). Second,

these postural tasks simply require postural maintenance regardless of the nature of the perturbation, whereas our task required participants to plan a movement towards one of multiple targets. Such movement planning appears to activate differential control of the gamma motor neurons to tune muscle spindle and reflex feedback to the upcoming movement (Papaioannou & Dimitriou, 2021). Such goal-directed modulation of stretch reflexes may reflect the development and tuning of feedforward predictive models, which Sainburg and colleagues proposed to be the case for the dominant limb (Bagesteiro & Sainburg, 2003; Sainburg, 2005, 2014; Sainburg & Kalakanis, 2000). Weaker goal-directed modulation in the non-dominant arm possibly reflects effective frugality in the control and/or maintenance of neural elements.

Goal-directed tuning of SLR gain is likely facilitated by changes in gamma drive. The old view that muscle spindle sensitivity is mainly associated with α–γ coactivation (Vallbo, 1970; Vallbo et al., 1979) is moving towards a more dynamic view where the fusimotor system allows advanced signal processing to occur at the periphery (Dimitriou, 2022). The observed effects of target direction and arm dominance on the SLR (and LLR) suggest that the dominant arm displays better independent fusimotor control. At the SLR epoch, we have found stronger goal-directed modulation of responses when the muscle is unloaded compared even with when there is no load applied to the limb. While such effects are most prominent in the dominant limb (Torell et al., 2023), we also find similar results here in the non-dominant limb following a longer preparatory delay. We hypothesize that this arises as the loading of the antagonists is accompanied by top-down reciprocal inhibition of lower motor neurons of the muscle, including gamma motor neurons (Dimitriou, 2014). This likely contributes to stronger goal-directed effects as the independent goal-directed control of dynamic gamma motor neurons occurs on top of this blanket reciprocal inhibition of lower motor neurons. Indeed, there is evidence that such goal-directed tuning of muscle spindles may occur primarily through changes in dynamic gamma drive to primary muscle spindles, as there is no evidence for preparatory goal-directed tuning of secondary muscle spindles (Papaioannou & Dimitriou, 2021).

5 | CONCLUSIONS

Overall, the current study supports previous findings that sufficient preparation before a planned movement and muscle unloading (i.e., antagonist loading) facilitates goal-directed modulation of stretch reflexes in both the short and long latency intervals (Papaioannou & Dimitriou, 2021; Torell et al., 2023). Here, we extend the

work by showing that goal-directed tuning of stretch reflexes is significantly reduced in the non-dominant limb compared with the dominant limb. Such differences may reflect the different control involved depending on limb laterality and highlight a potential role for independent gamma drive in the higher skill and function of the dominant limb. Our results suggest that the more sophisticated control of reflexive stiffness in the dominant limb, likely facilitated by superior fusimotor control, partly underpins the laterality of motor performance.

AUTHOR CONTRIBUTIONS

Conceptualization: Michael Dimitriou. *Data curation and formal analysis*: Michael Dimitriou, Frida Torell, Sae Franklin and David W. Franklin. *Funding acquisition*: Michael Dimitriou. *Resources*: Michael Dimitriou. *Methodology*: Michael Dimitriou and Frida Torell. *Visualization*: Michael Dimitriou and Frida Torell. *Writing—original draft*: Michael Dimitriou, Frida Torell, Sae Franklin and David W. Franklin. *Writing— review and editing*: Michael Dimitriou, Frida Torell, Sae Franklin and David W. Franklin.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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DATA AVAILABILITY STATEMENT

EMG data are available at Mendeley Data, V1, doi: 10.17632/4s28xcr6n6.1.

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