american
physiological
society®

JNP | **JOURNAL OF NEUROPHYSIOLOGY**®

RESEARCH ARTICLE

Control of Movement

Symbolic cues enhance express visuomotor responses in human arm muscles at the motor planning rather than the visuospatial processing stage

Samuele Contemori,[1] Gerald E. Loeb,[2] Brian D. Corneil,[3,4,5] Guy Wallis,[1] and Timothy J. Carroll[1]

[1]*Centre for Sensorimotor Performance, School of Human Movement and Nutrition Sciences, The University of Queensland, Brisbane, Australia;* [2]*Department of Biomedical Engineering, University of Southern California, Los Angeles, California;* [3]*Department of Physiology and Pharmacology, Western University, London, Ontario, Canada;* [4]*Department of Psychology, Western University, London, Ontario, Canada; and* [5]*Robarts Research Institute, Western University, London, Ontario, Canada*

Abstract

Humans can produce "express" (∼100 ms) arm muscle responses that are inflexibly locked in time and space to visual target presentations, consistent with subcortical visuomotor transformations via the tecto-reticulo-spinal pathway. These express visuomotor responses are sensitive to explicit cue-driven expectations, but it is unclear at what stage of sensory-to-motor transformation such modulation occurs. Here, we recorded electromyographic activity from shoulder muscles as participants reached toward one of four virtual targets whose physical location was partially predictable from a symbolic cue. In an experiment in which targets could be veridically reached, express responses were inclusive of the biomechanical requirements for reaching the cued locations and not systematically modulated by cue validity. In a second experiment, movements were restricted to the horizontal plane so that the participants could perform only rightward or leftward reaches, irrespective of target position on the vertical axis. Express muscle responses were almost identical for targets that were validly cued in the horizontal direction, regardless of cue validity in the vertical dimension. Together, these findings suggest that the cue-induced enhancements of express responses are dominated by effects at the level of motor plans and not solely via facilitation of early visuospatial target processing. Notably, direct corticotectal and corticoreticular projections exist that are well-placed to modulate prestimulus motor preparation state in subcortical circuits. Our results could reflect a neural mechanism by which contextually relevant motor responses to compatible visual inputs are rapidly released via subcortical circuits that are sufficiently along the sensory-to-motor continuum.

NEW & NOTEWORTHY Express arm muscle responses to suddenly appearing visual targets for reaching rapid have been attributed to the tecto-reticulo-spinal pathway in humans. We demonstrate that symbolic cues before target presentation can modulate such express arm muscle responses compatibly with the biomechanics of the cued reaching direction and the cue validity. This implies cortically mediated modulation of one or more sensorimotor transformation nodes of the subcortical express pathway.

motor preparation; reticular formation; stimulus-locked response; subcortical motor control; superior colliculus

INTRODUCTION

Reaching for objects requires neural computations to evaluate the surrounding context and transform the sensory information into appropriate agonist/antagonist muscle responses to bring the hand to the target (1–3). In behavioral neuroscience, the time required by the brain to initiate a visually guided action is often inferred from the stimulus-to-movement delay (i.e., reaction time, RT) (4).

The time that agonist and antagonist muscles take to produce enough force to start the movement, however, is longer than the premotor muscle response [i.e., earliest divergence of the electromyographic (EMG) signal from background]. Therefore, EMG measurements can provide earlier evidence of the visuomotor processes at play during a target-directed reaching task than RTs.

Interestingly, previous EMG work showed that humans can produce extremely fast stimulus-driven arm muscles responses

that are inflexibly locked in space and time to visual stimuli (5–18), which were originally termed stimulus-locked responses (SLRs) (5). Specifically, the SLRs consistently encode the location of a visual stimulus within ~100 ms from its presentation, irrespective of the mechanical RT. The SLRs hence lack the typical trial-by-trial variability of volitional muscle response and ensuing RT that is due to multiple external and internal factors (e.g., number of choices, attention, motivation, and expectation). This suggests that the visuomotor pathway for this specific class of short-latency stimulus-locked responses differ from longer-latency "movement-locked" muscle responses. Indeed, the neural pathway for SLRs has been hypothesized to parallel that of express saccades (19), which involves the superior colliculus and its downstream projection to the reticular formation (20–24). Consequently, we and others have referred to short-latency EMG responses observed within the established "SLR" time window as "express" arm muscles responses (16–18) and will use this terminology here.

Express arm muscle responses were recently shown to be modulated by temporal expectations about the stimulus (16), suggesting a top-down cortical modulation of the putative subcortical express pathway. In addition, Contemori et al. (17) showed that explicitly cueing the target location with a symbolic arrow-shaped cue promoted or impaired express muscle responses to cued or noncued targets, respectively. This could reflect top-down influence on express muscle response via modulation of cue-driven sensory or motor processing. In the first case, the cue might direct attention to the expected target location in the visual field thus facilitating sensory-to-motor transformation of validly cued targets. In the second case, the cue might enhance pretarget motor preparation of the expected reach such that express muscle responses are facilitated when a compatible target appears. Here, we ran two experiments to dissociate these possible mechanisms underlying the cue-induced modulations of express arm muscle responses in humans. Furthermore, we implemented and validated a novel method of analysis to discriminate express muscle responses in individual trials. Notably, we developed this method to overcome some limits of the time-series receiver operator characteristic (ROC) analysis that has been previously adopted to detect express muscle responses (5, 16, 17) (see MATERIALS AND METHODS for further details).

In the first experiment, participants reached toward one of four potential targets that were projected virtually in the horizontal plane, thus requiring different mechanical contributions from the recorded muscles to reach the four target locations. Specifically, the target could appear above or below a fixation spot either to the left or right of fixation. Trial-by-trial, the target location was partially predictable from a symbolic arrow-shaped cue oriented toward one of the four possible target locations. If the cue modulates early visuospatial processing, then express muscle responses should be facilitated and impaired by valid and invalid cues, respectively. However, we found that express muscle responses were modulated according to the mechanical output required to reach toward the cued direction, rather than strictly based on the cue validity. This suggests that the cue-induced modulations of express responses act, at least partly, at the level of motor plans along the putative subcortical express pathway, rather than solely via facilitation of early sensorimotor transformations at cued spatial location.

We next tested whether cueing the likely target location influences express visuomotor behavior via purely visuospatial mechanisms, in addition to any effect on motor preparation. We used a cued-target paradigm akin to that of the first experiment, but here the targets were projected virtually in the vertical plane while reaching movements were restricted to the horizontal plane. If facilitation of visuospatial target processing contributes strongly to cue-enhanced express behavior, then validly cueing the vertical location of the target should have facilitated express responses even if this prior information was relevant only to identify the location in the visual field. In contrast, we observed almost identical express arm muscle responses for targets that were compatible with the cued reaching direction, regardless of cue validity in the vertical dimension.

Overall, our results appear to reflect a contribution of top-down motor preparation to express arm muscle responses, such that there is rapid integration of motor plans for anticipated movements with emerging visual inputs along the putative subcortical express pathway. Such an arrangement could facilitate rapid release of prepared motor actions in response to compatible visual stimuli.

MATERIALS AND METHODS

Participants

Fifteen adults participated in the first experiment (3 females; mean age: 29.3 ± 7.3 yr), and 11 of them also participated in the second experiment that had a total sample of 16 adults (2 females; mean age: 28.9 ± 7.7 yr). All participants were right-handed, had normal or corrected-to-normal vision, and reported no current neurological or musculoskeletal disorders. They provided informed consent and were free to withdraw from the experiment at any time. All procedures were approved by the University of Queensland Medical Research Ethics Committee (Brisbane, Australia) and conformed to the Declaration of Helsinki.

Task Design and Experimental Setup

Task design.

We used an emerging moving target paradigm (Fig. 1A) that has proven effective to facilitate the express visuomotor arm muscle responses (14–18). In both experiments, the target was a filled black (~0.3 cd/m²) circle of ~2 degrees of visual angle (dva) in diameter presented against a light gray background (~140 cd/m²). This created a high target-to-background contrast necessary to facilitate the generation of express arm muscle responses (6, 15). The luminance was measured with a colorimeter (Cambridge Research System ColorCAL MKII). A photodiode was attached to the left bottom corner of the monitor to detect a secondary light that was presented coincidentally with the time of appearance of the real target. This allowed us to index the time point at which the stimulus was physically detectable. Note that the secondary light was not visible by the participants as it was fully occluded by the photodiode.

The participants performed visually guided reaches toward the targets whose location was partially predictable from the orientation of a symbolic arrow-shaped cue (Fig.
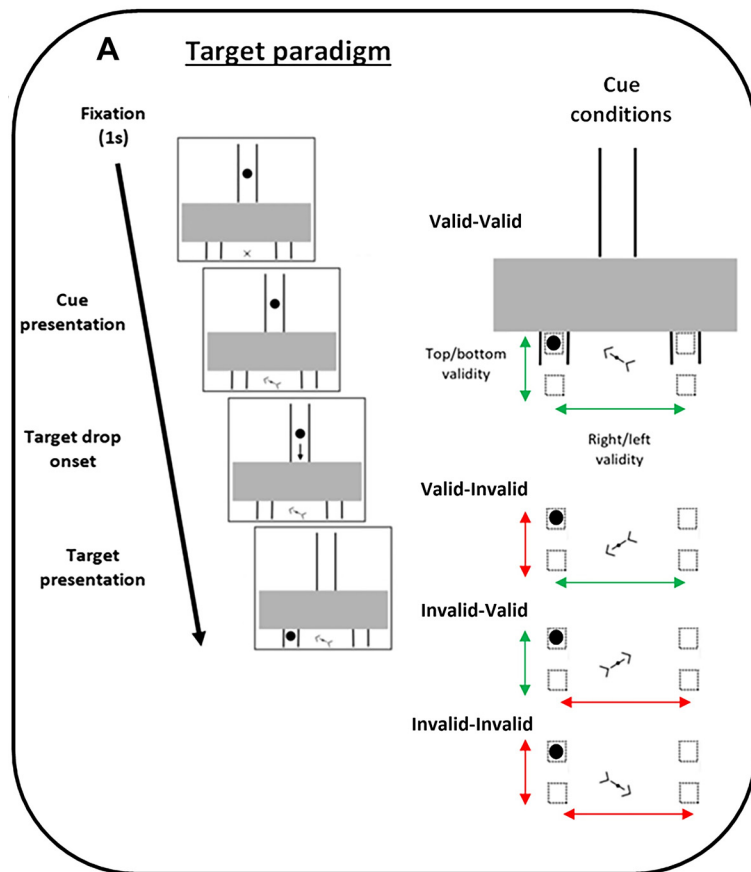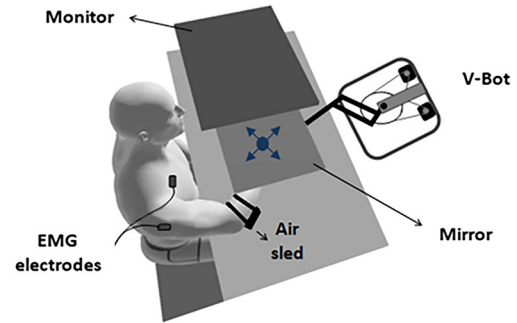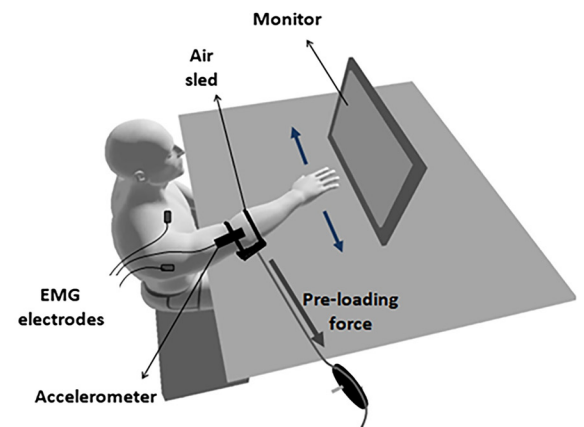
Figure 1. *A*: schematic diagram of the timeline of events in the target paradigm; a zoomed view of the paradigm and cue attributes are shown in the top left corner (the dashed boxes indicate the four possible locations of the target). After one second of fixation, the central "X" sign for fixation was substituted by an arrow cue pointing validly or invalidly toward the target location. After ~700 ms from cue presentation, the target started dropping from the stem of the track at constant velocity of ~35 degrees of visual angle (dva)/s until it passed behind the barrier (i.e., occlusion epoch) for ~480 ms, and reappeared underneath it at ~640 ms from the its movement onset time either when it reemerged just beneath the barrier (i.e., top targets) or closer to the bottom of the screen (i.e., bottom targets; 17). The target appeared transiently by making one single flash of ~8 ms of duration. The cue had two levels of validity: right/left and top/bottom (the cue validity and invalidity are shown with green and red arrows, respectively). The right column of panels shows the four cue-orientation variations relative to the target that appeared to the left and just beneath the barrier (i.e., top-left target). *B*: first experiment experimental setup. Participants' hand positions were virtually represented via a cursor (blue dot) displayed on the monitor and projected into the (horizontal) plane of hand motion via a mirror. The head position was stabilized by a forehead rest (not shown here). The blue arrows represent the four reaching directions to address each of the four possible targets. *C*: second experiment experimental setup. In both experiments, participants were seated and began with their dominant (right) hand aligned with the fixation spot ("X" sign beneath the barrier, see *A*) and moved it toward a target that appeared beneath the barrier. Head position was stabilized by chin and forehead rests (not shown here). The blue arrows represent the rightward and leftward horizontal upper limb movements that participants could execute to address the location of one of the four possible targets (i.e., two possible movements for four possible targets).

1A). The cue-target onset asynchrony (CTOA) was >1 s to ensure unambiguous interpretation of the arrow orientation. For both experiments, the target was constrained to fall within a track, which was shaped as an inverted diapason, until it passed behind a visual barrier that occluded the junction point at which the target randomly deviated left or right (16, 17). The target reappeared transiently (one single flash of ~8 ms of duration) at one of four different locations underneath the barrier: *1*) to the right, just beneath the barrier (i.e., top-right location); *2*) to the right, closer to the bottom of the monitor (bottom-right location); *3*) to the left, just beneath the barrier (i.e., top-left location); *4*) to the left, closer to the bottom of the monitor (bottom-left location).

To start the trial, the participants were instructed to align their right hand (or the cursor in the first experiment; Fig. 1B) and the gaze at a central "X" sign underneath the barrier (Fig. 1A), and to stare at it for 1 s. After the fixation period, the central fixation spot was changed to a symbolic inclined arrow oriented toward one of the four possible target locations. In both experiments, the arrow validly cued the target location in ~70% of the trials (see the following sections for details about the cue validity). Note that symbolic meaning was derived from the orientation and shape of the cue, whereas its physical position was uninformative for the future target location. The cue informed the subjects about the likely right/left and top/bottom locations of the target,

thus providing two levels of cue validity. There were four different cue conditions (right column of panels in Fig. 1A): 1) "Valid-Valid," when both the right/left and top/bottom target locations were validly cued; 2) "Valid-Invalid," when only the right/left target location was validly cued; 3) "Invalid-Valid," when only the top/bottom target location was validly cued; 4) "Invalid-Invalid," when neither the right/left nor the top/bottom target locations were validly cued.

Experiment 1: Experimental setup.

Here, we tested cue-induced modulations of express visuomotor responses when the four target locations could be reached via distinct and veridical movements. To this aim, we used a two-dimensional planar robotic manipulandum (the vBOT) (25). The target was displayed on an LCD computer monitor (120 Hz refresh rate; $8.\overline{33}$ ms/refresh cycle) mounted above the vBOT handle and projected to the participant via a mirror (Fig. 1B). The stimuli were created in Microsoft Visual C++ (Version 14.0, Microsoft Visual Studio 2005) using the Graphic toolbox. The handle position was virtually represented by a blue cursor (~1.2 dva) whose apparent position coincided with actual hand position in the plane of the limb (i.e., top and bottom targets were physically distinguished by their depth relative to the body). The targets were located at 60°, 120°, 240°, and 300° around the fixation spot (distance between top and bottom targets: 5.5 cm; distance between right and left targets at the same depth: 10 cm) and had equal eccentricity of ~10 dva from the fixation spot. A constant rightward load of ~5 N was applied to preload the shoulder transverse flexor muscles, including the clavicular head of pectoralis major muscle, and a custom-built air sled was positioned under the right elbow to minimize sliding friction (16, 17). The participants had to gaze at the fixation spot until the target reappeared from behind the barrier (a "fixation" error was shown if this condition was not met and the trial was reset), and then to start moving as rapidly as possible toward the target. Horizontal gaze-on-fixation was checked online with bitemporal, direct current electrooculography (EOG) sampled at 1 kHz. Each participant completed 15 blocks of 80 reaches/block (20 for each of the 4 target locations), with each block consisting of 56 Valid-Valid, 8 Valid-Invalid, 8 Invalid-Valid, and 8 Invalid-Invalid cue trials, randomly intermingled (see *Task design* and Fig. 1A for further details). Therefore, the arrow validly cued the target location on 70% of the trials.

Experiment 2: Experimental setup.

Here, we tested the influence of prior information on express visuomotor responses toward the same four targets (Fig. 1A) that, however, were distributed among the horizontal (right/left targets) and vertical (top/bottom targets) dimensions while the arm could move only horizontally such that it could not match the target vertical locations. To this aim, we used an experimental setup previously described by Contemori et al. (16, 17) and illustrated in Fig. 1C. The participant executed right (extensor-ward) or left (flexor-ward) horizontal upper limb movements in response to targets presented at the four possible locations that were displayed on an LCD monitor (120 Hz refresh rate; $8.\overline{33}$ ms/refresh cycle) positioned vertically ~57 cm in front of the participants (distance between top and bottom targets: 8 cm;

distance between right and left targets: 15 cm). Again, we preloaded (~5 N) the shoulder transverse flexor muscles and positioned a custom-built air sled under the right elbow to reduce movement friction. The stimuli were created in MATLAB (v. R2014b, The MathWorks, Inc., Natick, MA) using the Psychophysics toolbox (26, 27). The participants were instructed not to move their eyes from the fixation spot until the target reappeared from behind the barrier, and to reach as fast as possible toward the target. If the fixation condition was not met, the participants received an error message and the trial was reset. Gaze-on-fixation was checked online with an EyeLink 1000 plus tower-mounted eye tracker device (SR Research Ltd., Ontario, Canada), at a sampling rate of 1 kHz. Each participant completed 10 blocks of 68 reaches/block (17 for each of the 4 target locations) comprising: 40 Valid-Valid cues; 12 Valid-Invalid cues; 8 Invalid-Valid cues; and 8 Invalid-Invalid cues. Therefore, the arrow cued the right/left target location with ~75% validity, whereas the top/bottom location was cued with ~75% validity for valid right/left cue conditions and 50% validity for invalid right/left cue conditions. The four cue conditions were randomly intermingled within each block.

Data Recording and Analysis

Kinematic data.

For the first experiment, we reconstructed the hand movements (Fig. 2A) by using the vBOT handle kinematic data sampled at 1 kHz. An error message was shown online if the cursor left the starting position within 130 ms from the stimulus presentation (17). This RT cutoff was adopted because 130 ms was recently shown to be the critical time to prepare a target-directed response (28). The RT for analysis was computed offline by identifying the first time point at which the radial (rho) hand velocity exceeded the baseline mean velocity (i.e., average velocity recorded from 100 ms before the target presentation to the stimulus onset time) by more than five standard deviations (Fig. 2B). Critically, for trials faster than 130 ms, the EMG signal enclosed in the express epoch could be polluted by the muscle response locked to the volitional RT. Moreover, consistent with previous work (17), we adopted an even more conservative RT cutoff of 140 ms (~9%) from offline analysis, in addition of those with RT > 500 ms (<1%).

To determine the correct (i.e., target-directed) reaches, we recorded the *X* and *Y* hand position at the RT and when the hand reached 75% of the peak velocity (Fig. 2C). We then computed the angle of a line passing between these hand positions to define the initial movement direction (Fig. 2A). If the initial movement was directed within the quadrant of the visual field containing the target, we concluded that the movement was correct, otherwise the movement was classified as incorrect and not further analyzed.

To test whether the target-directed reach was modulated by the cue, we computed the angle error between the actual initial hand-to-target trajectory (see the previous paragraph) and the "optimal" hand-to-target trajectory. The optimal trajectory was defined by computing the angle of the line passing from the hand position at the RT and the target position. Note that the target position was corrected relative to the hand position at the RT, which on average was ~0.5 cm away from the "home" position. For each of the four target
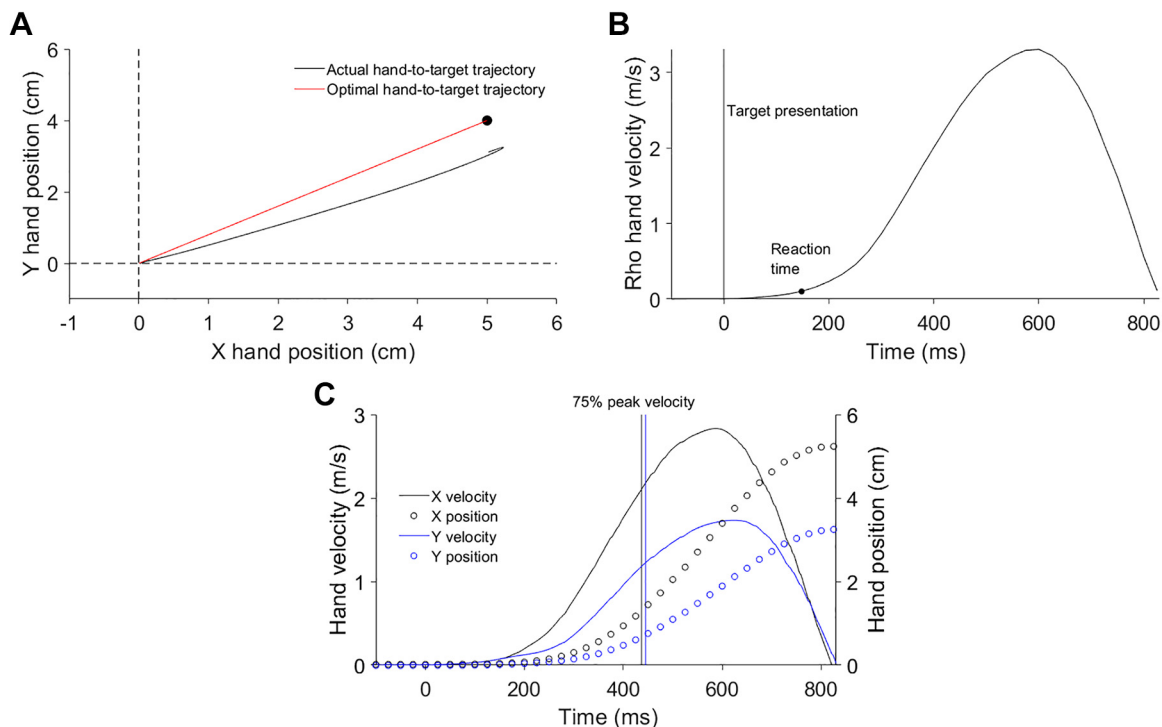
Figure 2. Kinematic analysis procedures for an exemplar valid cue trial. The movement was directed toward the target that appeared at the right of the fixation spot and just beneath the barrier (i.e., top-right target; see Fig. 1*A*). *A*: actual (black trace) and optimal (red trace) hand reaching trajectories in the medio-lateral (*X*) and backward-forward (*Y*) axes from the [0,0] "home" position toward the target location (black dot). In this example, the initial trajectory was directed slightly more horizontally than the optimal target trajectory thus leading to a positive initial trajectory error. *B*: profile of the radial (rho) hand velocity used to index the reaction time of the movement after the target presentation. The rho hand velocity was obtained by computing the root-mean-square of the square of sums of the hand velocity of the medio-lateral and backward-forward directions. *C*: profiles of the hand velocity (solid lines) and trajectory (dotted lines) in the medio-lateral (*X*; black lines) and backward-forward (*Y*; blue lines) directions. The hand position coordinates at the reaction time and at 75% of the peak velocity in the *X* and *Y* axes (vertical lines) were used to determine the initial trajectory direction and the trial correctness. This trial was correct because the initial reach was directed within the quadrant of the visual field containing the target (see *A*).

locations, negative angle errors indicate that the initial movement was further away from the horizontal midline between targets than the optimal target trajectory. By contrast, positive angle errors indicate that the initial reaching was closer to the horizontal midline between targets than the optimal target trajectory (Fig. 2*A*).

For the second experiment, the arm motion was monitored by a three-axis accelerometer (Dytran Instruments, Chatsworth, CA) sampled at 2 kHz with a 16-bit analog-digital converter (USB-6343-BNC DAQ, National Instruments, Austin, TX). Data synchronization was guaranteed on each trial by starting the recording at the frame at which the target started moving toward the barrier. We monitored the RT online (see Ref. 17 for details) and sent an error message if the participants moved before the target onset time or responded in <130 ms from target presentation. The accelerometer signal was also used for offline RT computation and for the identification of correct (i.e., target-directed) responses (see Refs. 16 and 17 for details). Consistent with the first experiment, trials with RT < 140 ms (~10%) and >500 ms (<1%) were once again excluded during offline data analysis.

For both experiments, the kinematic data were averaged across the left and right directions to limit biases related to the preload. This was done separately for the top and bottom targets (i.e., kinematic data were pooled for right-up and left-up targets, and for right-down and left-down targets).

EMG data.

Surface EMG activity was recorded from the clavicular head of the right pectoralis muscle (PMch) and the posterior head of the right deltoid muscle (PD) with double-differential surface electrodes (Delsys Inc. Bagnoli-8 system, Boston, MA). Before the start of recording, we checked the quality of the EMG signal with an oscilloscope by asking the participants to flex (PMch activation-PD inhibition) and extend (PMch inhibition-PD activation) the shoulder in the transverse plane. The sEMG signals were amplified by 1,000, filtered with a 20–450 Hz bandwidth filter by the "Delsys Bagnoli-8 Main Amplifier Unit," and sampled at 2 kHz using a 16-bit analog-digital converter (USB-6343-BNC DAQ device, National Instruments, Austin, TX). Trial-by-trial, the quality of the EMG signal was verified online on the experimenter's computer via a custom MATLAB script that generated live plots of the recorded data, thus allowing us the opportunity to interrupt the experiment in case of low signal quality or electrode connection lost. The sEMG data were then downsampled to 1 kHz and full-wave rectified offline without further filtering.

We and others have previously adopted a time-series ROC analysis to determine the earliest stimulus-related muscle response (5, 16, 17). This analysis, however, is sensitive to the muscle response amplitude relative to the background signal-to-noise ratio, which is influenced by

the sample size. Critically, Cross et al. (29) reported non-physiological short-latency muscle responses (<60 ms) to visual perturbation of the cursor position when the ROC analysis was run on ~10 trials. This calls into question the reliability of the ROC analysis for small data samples. In our experiments, relatively few trials (~25) were run in the invalid cue condition and trials with reaction times <140 ms or >500 ms and incorrect movements were excluded (see the *Kinematic data section*). Note also that the ROC analysis is run on the entire data set to index the first point in time at which the target location can be discriminated solely from the EMG signal. Critically, this temporal value is biased by the relative amount of express and long-latency muscle responses (e.g., discrimination times > 120 ms for samples with a low occurrence of express muscle responses). The ROC, therefore, does not provide information about the percentage of express versus long-latency muscle responses within a full data set and the physiological trial-by-trial variability of the earliest stimulus-driven muscle response and. For these reasons, we developed a single-trial analysis method to extract the muscle response onset time from each correct trial (named the detrended-integrated signal method), which is described below and illustrated in Fig. 3. The ROC analysis was run, however, on the cue conditions with a large number of trials (i.e., Valid-Valid cue conditions; see previous paragraph) to test the statistical contrasts between the two methods (Supplemental Materials and Methods; all Supplemental Material is available at https://doi.org/10.17605/OSF.IO/75JT2.

To index the earliest stimulus-related muscle response from each correct trial, we first subtracted the background activity value (i.e., average rectified EMG signal recorded from 100 ms before to 70 ms after the stimulus presentation) from the entire EMG signal (Fig. 3, A and D). This allowed us to reduce the rising trend of the signal obtained by computing the integral of the EMG trace for each millisecond recorded between 100 ms before and 300 ms after the target onset time (gray trace in Fig. 3, B and E). We further detrended the signal by subtracting the linear regression function of the background period (magenta line in Fig. 3, B and E) from the entire 400 ms analysis window (black line in Fig. 3, B and E). We then computed the average (dotted lines in Fig. 3, C and F) and standard deviation values of the detrended-integrated signal in the background period. We indexed the candidate muscle response onset time (unfilled black dot in Fig. 3, C and F) as the first time the detrended-integrated signal exceeded the background value by more (i.e., earliest muscle activation), or less (i.e., earliest muscle inhibition), than five standard deviations (dashed lines in Fig. 3, C and F). Importantly, the occurrence of false-positive express muscle responses (i.e., candidate onset times earlier than 70 ms after the target presentation) was lower than 5% with this threshold. Critically, the candidate response onset time is sensitive to the amplitude of the stimulus-driven response relative to the background activity and does not exactly correspond to the actual initial deviation of the EMG signal from background. To find this point in time, we ran a linear regression analysis around the candidate onset time of the stimulus-driven muscle response. Specifically, if the signal at the candidate onset time was higher than background, we extrapolated the linear trendline from the values

enclosed between the last valley before and the first peak after the candidate onset time (Fig. 3C). By contrast, if the signal at the candidate onset time was lower than background, the linear trendline was computed from the values enclosed between the last peak before and the first valley after the candidate onset time (Fig. 3F). Finally, we defined the muscle response onset time as the point in time the linear trendline intercepted the background value of the detrended-integrated signal (vertical line in Fig. 3, A–F). Consistent with previous work (7, 16, 17), we defined the muscle response as "express" if it was initiated within 70–120 ms after the target presentation.

Express muscle responses appear as a column of muscle activation (Fig. 3G) or inhibition (Fig. 3H) at ~100 ms after the stimulus onset time that does not covary with the voluntary movement initiation. In the absence of express responses, the earliest EMG responses (activation or inhibition) occur at times that covary with the RT (Fig. 3, I, J, M, and N).

To produce an objective measure for this distinction, we selected the trials showing an express muscle response and we binned them in "express-fast" and "express-slow" trial sets according to the median RT value of the full class of express trials. We then computed the average express responses initiation time of the express-fast and express-slow trial sets as well as the average RT of the corresponding fast and slow trial sets. Finally, we fitted a line to the data to test if the muscle response onset time did not covary with the RT. Specifically, for each participant we classified a data set as positive for an express muscle response if the slope of the line was >67.5° (5, 6, 16, 17). If express responses were positively detected for a data set, we computed the average muscle response initiation time and express response prevalence (%) across the individual trials within the data set with EMG onset times within the express muscle response window. We also quantified the express response magnitude by computing the average EMG activity recorded in the 10 ms subsequent to the response initiation time for each rightward and leftward trial exhibiting an express muscle response. We then averaged this metric across the express response trials and computed the difference between the left and right targets. Note that these procedures were run separately for the top targets and the bottom targets to test the contrast between targets at comparable vertical locations.

Statistical Analysis

Repeated-measures ANOVA analyses with Bonferroni correction were conducted in SPSS (IBM SPSS Statistics for Windows, v. 25, SPSS Inc., Chicago, IL) as the normality of the distributions was verified by the Shapiro–Wilk test. ANOVA analyses were conducted with cue condition (4 levels: Valid-Valid, Valid-Invalid, Invalid-Valid, and Invalid-Invalid) and target location on the vertical axis (2 levels: top and bottom) as within-participant factors, unless otherwise stated. When the ANOVA revealed a significant main effect or interaction, we computed the partial eta squared (η_p^2) to estimate the effect size and ran Bonferroni tests for post hoc comparisons. Correlation analyses were conducted with Pearson correlation tests. For all tests, the statistical significance was designated at $P < 0.05$.

To test the statistical contrast in express response initiation time between the detrended-integrated signal and ROC analyses, we used single-subject statistical analysis (Supplemental Materials and Methods). For the detrended-integrated signal analysis, we also used this statistical approach to test the contrast in express response initiation time between the four different cue conditions at the single-subject level (Supplemental Materials and Methods; see Refs. 16 and 17 for further details).

RESULTS

Experiment 1

Task correctness, reaction time, and kinematics.

The cue validity had a significant effect on the prevalence of correct target-directed reaches ($F_{3,14} = 23.3$, $P < 0.001$, $\eta_p^2 = 0.63$). For both the top and bottom targets, the proportion of correct reaches was significantly higher when the target
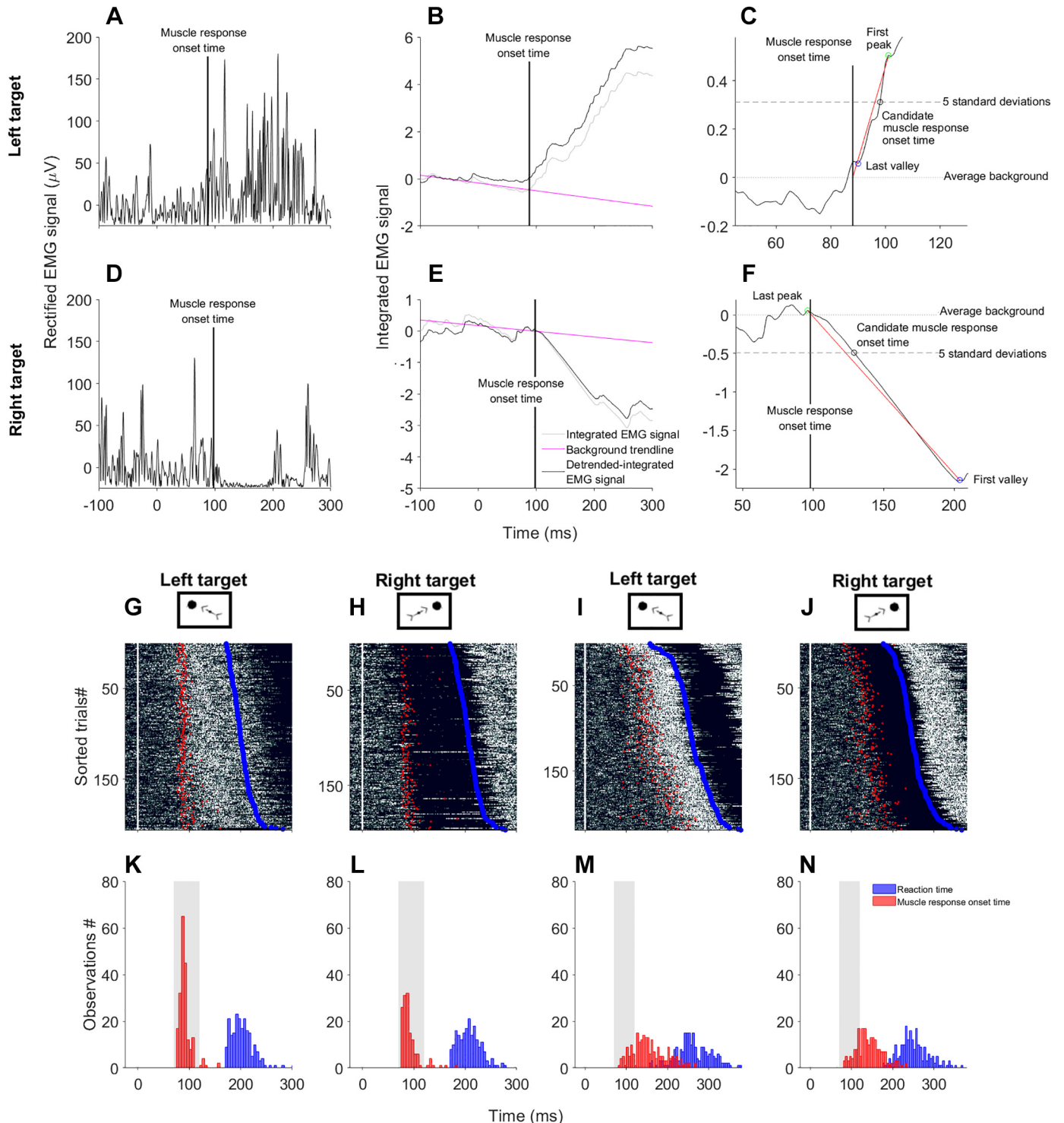
Table 1. *Percentage of correct target-directed reaches toward top and bottom targets in the two experiments*

| | Cue Conditions | | | |
	Valid-Valid	Valid-Invalid	Invalid-Valid	Invalid-Invalid
Experiment 1				
Top target (%)	98.8 ± 1*'**'***	76.1 ± 16.6 + +	82.9 ± 10.9	86.6 ± 9.8
Bottom target (%)	98.3 ± 2.6*'**'***	76.4 ± 15 + +	84.3 ± 11.7	86.8 ± 9.5
Experiment 2				
Top target (%)	96.3 ± 3.5**'***	95.9 ± 4.4 +'+ +	89.6 ± 6.4	86.6 ± 9.2
Bottom target (%)	95.1 ± 3.8**'***	95.4 ± 4.4 +'+ +	86.6 ± 9.4	86.6 ± 8.5

Statistically significant difference between the Valid-Valid cue condition: *the Valid-Invalid cue condition; **the Invalid-Valid cue condition; ***the Invalid-Invalid cue condition. Statistically significant difference between the Valid-Invalid cue condition and: +the Invalid-Valid cue condition; + +the Invalid-Invalid cue condition. Data reported as means ± standard deviation.

location was validly than invalidly cued (Table 1). Furthermore, significantly fewer correct trials were observed in the Valid-Invalid than Invalid-Invalid cue conditions (Table 1). This indicates that providing invalid cues promoted incorrect reaching directions.

The first line of panels in Fig. 4 shows exemplar correct reaching trajectories from a single participant toward the top-right target. For this person, the RT was ~200 ms when the target was validly cued, ~240 ms when only the right/left target location was validly cued, and ~280 ms whenever the right/left cue orientation was invalid (Fig. 4E). The initial trajectory angle errors were larger in the Valid-Invalid cue condition (~15°) than in the other cue conditions (~7°; Fig. 4F). In the example used in Fig. 4B, this would indicate that the initial reach direction was biased more from the target direction (i.e., top-right) toward the cued direction (i.e., bottom-right) than was observed for the other cue conditions. Moreover, a strong negative correlation ($r = -0.76$; Fig. 4G) between the initial trajectory angle error and RT was observed only for the Valid-Invalid cue condition, which indicates that the shorter the movement onset time the greater the cue-induced bias on the initial movement trajectory.

For the entire group, the RT was significantly influenced by the cue-condition ($F_{3,14} = 75.3$, $P < 0.001$, $\eta_p^2 = 0.84$) and the target location on the vertical axis ($F_{1,14} = 28$, $P < 0.001$, $\eta_p^2 = 0.667$), and by their interaction ($F_{3,14} = 2.9$, $P = 0.048$, $\eta_p^2 = 0.2$). For both the top and bottom targets, the RT was significantly shorter when the target location was validly than invalidly cued (Fig. 5, A and D). The RT was also significantly shorter in

the Valid-Invalid cue condition than the Invalid-Valid and Invalid-Invalid cue conditions (Fig. 5, A and D).

The initial trajectory angle error was significantly influenced by the cue-condition ($F_{3,14} = 10.8$, $P < 0.001$, $\eta_p^2 = 0.43$) and by the target location on the vertical axis ($F_{1,14} = 13.7$, $P = 0.002$, $\eta_p^2 = 0.49$), and by their interaction ($F_{3,14} = 3.6$, $P = 0.045$, $\eta_p^2 = 0.2$). For the top target, the initial trajectory error was larger in the Valid-Invalid cue condition than in the other cue conditions (Fig. 5B). A similar trend between the four cue conditions was observed also for the bottom target (Fig. 5E), even though these contrasts were not statistically significant. Furthermore, for the correlation coefficient between the initial trajectory error angle and RT the ANOVA showed a significant main effect for cue condition ($F_{3,14} = 14.2$, $P < 0.001$, $\eta_p^2 = 0.5$). Note that similar results were obtained by running the ANOVA analysis on correlation coefficients transformed via the Fisher z-transformation procedure. For both the top and bottom targets, the correlation coefficient was significantly more negative for the Valid-Invalid cue condition than the other cue conditions (Fig. 5, C and F).

In all, these data indicate that the valid right/left cues facilitated the RT. Validly cueing only the horizontal target location (i.e., Valid-Invalid cue conditions), however, also biased the initial movement toward the invalid top/bottom cued location. Critically, the initial trajectory angle error in the Valid-Invalid cue condition increased as participants reduced their RT, which justifies the larger prevalence of incorrect (i.e., non-target-directed) responses for the Valid-Invalid than other invalid cue conditions.

Figure 3. Detrended-integrated signal method. The first two lines of panels show the procedures for an exemplar left target trial and an exemplar right target trial that were executed toward validly cued top targets. *A* and *D*: the pectoralis muscle (clavicular head) rectified EMG activity after the subtraction of the average background EMG value. *B* and *E*: the integrated EMG signal (gray traces) as well as the detrended-integrated EMG signals obtained after having subtracted the background trendline (magenta line) from the integrated electromyographic (EMG) signal. A zoomed view of the detrended-integrated EMG signals is shown in (*C*) and (*F*) as are the average (dotted gray line) and five standard deviations (dashed gray lines) values of the detrended-integrated EMG signal in the background period. In these panels, the black unfilled scatter indicates the time at which the detrended-integrated signal diverges from background by more (*C*) or less (*F*) than five standard deviations, which represents the candidate onset time of the express visuomotor muscle response. The green and blue unfilled scatters represent the boundaries of the time-window of data from which we computed the linear trendline (red line) that was used to index the point in time the linear trendline intercepted the background value of the detrended-integrated signal (solid vertical line in *A–F*), which represents the earliest muscle response initiation time. In these examples, the linear trendlines intercepted the background value of the detrended-integrated signal within 70–120 ms (88 ms for the left target; 98 ms for the right target) after the target presentation and, thereby these trials were classified as express visuomotor muscle responses. Rasters of rectified surface EMG activity from individual trials are shown in *G–J* (brighter white colors indicate greater EMG activity). The white vertical line at 0 ms indicates the target presentation time, the muscle response initiation time is represented with a red scatter and the blue scatters indicate the reaction time. *K–N*: distribution of muscle response onset time (red histograms) and reaction time (blue histograms), and the gray path indicates the time window in which an express muscle response is expected (70–120 ms from target onset). The exemplar data shown in (*G*) and (*H*) are representative of an express muscle response producer because the earliest muscle responses appear as a vertical band of either muscle activations (*G*) or inhibitions (*H*) that is time locked ~100 ms to the stimulus onset time, regardless of the movement onset time. Consistently, the distribution of the muscle response onset time is mostly enclosed within the 50 ms express response time window (gray path in *K* and *L*) and does not match the spread of volitional movement onset times. By contrast, *I* and *J* represent a nonexpress muscle response because the muscle response onset time and reaction time are similarly distributed (*M* and *N*).

Figure 4. Correct target-directed reaching trials toward the top-right target of an exemplar subject from the first experiment. *A–D*: reaching trajectories for the Valid-Valid (green traces), Valid-Invalid (blue traces), Invalid-Valid (black traces), and Invalid-Invalid (red traces) cue conditions. For each cue condition, one variation of the cue orientation relative to the target location is shown in the framed squares. *E*: distribution of the reaction time for each of the four different cue conditions. *F*: distribution of the initial trajectory angle errors for each of the four different cue conditions. *G*: relationship between the reaction time and the initial trajectory angle error (*r* = Pearson correlation coefficient).
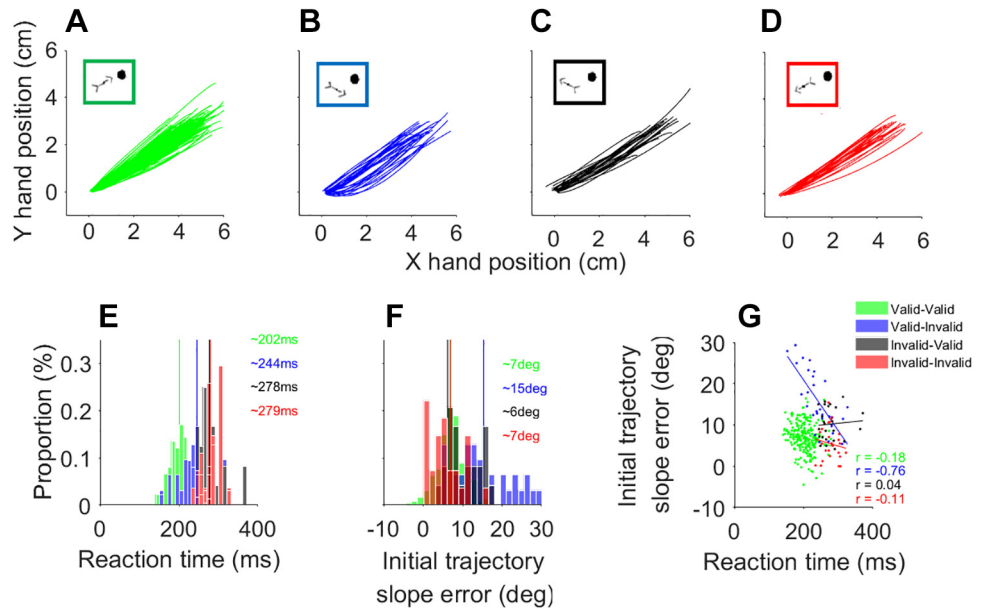
Express muscle response.

For the first experiment, 12 participants of 15 (80%) met the criteria for positive express response identification in each of the four cue conditions (see MATERIALS AND METHODS) on the PMch muscle. By contrast, the conditions for positive express-response determination on the PD muscle among each different cue condition were not met by any participant. The discrepancy between the PMch and PD muscles is consistent with previous work (16, 17) and is probably due to the preload, which enhanced solely the activity of the PMch muscle. Given the low occurrence of express responses for the PD, only the PMch was considered for statistical analyses.

Figure 6 shows surface EMG recordings from the PM muscle of an exemplar express response producer from the first experiment. For this subject, the percentage of express

response trials was higher when the right/left target location was validly (top target: Valid-Valid cue condition 69%, Valid-Invalid cue condition 65%; bottom target: Valid-Valid cue condition 75%, Valid-Invalid cue condition 72%) than invalidly cued (top target: Invalid-Valid cue condition 60%, Invalid-Invalid cue condition 44%; bottom-target: Invalid-Valid cue condition 64%, Invalid-Invalid cue condition 54%). For the top target, the muscle started encoding the target location at 90 ms from its presentation when it was validly cued, at 95 ms when only the right/left target location was validly cued (i.e., Valid-Invalid cue condition), and after 100 ms when the target appeared opposite to the cued right/left visual hemi field (i.e., Invalid-Valid and Invalid-Invalid cue conditions). For the bottom target, the express response initiation time was ∼90 ms when the right/left target

Figure 5. Metrics of the long-latency visuomotor behavior of the first experiment. Latency of correct reaches in the four different cue conditions for the *top* (*A*) and *bottom* (*D*) targets. Angle error between the optimal and actual initial trajectory of the movement (see MATERIALS AND METHODS, and Fig. 2 for details) in the four different cue conditions for the top (*B*) and bottom (*E*) targets. Note that the positive trajectory error angles indicate that the initial movement was directed more horizontally than the optimal target-directed trajectory. Correlation between the reaction time and the angle error of the initial trajectory (see MATERIALS AND METHODS, and Fig. 4G) for the top (*C*) and bottom (*F*) targets. Each black line represents one participant and the bars represent the mean across subjects. Note that the exemplar cue conditions outlined above the bars represent only top (*A–C*) and bottom (*D–F*) left target conditions for clarity. *Statistically significant differences between the cue conditions.
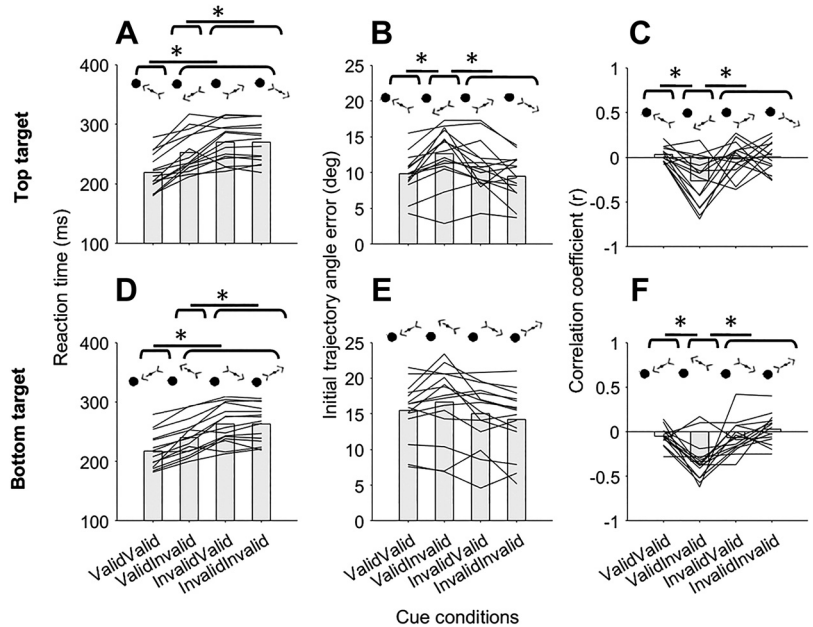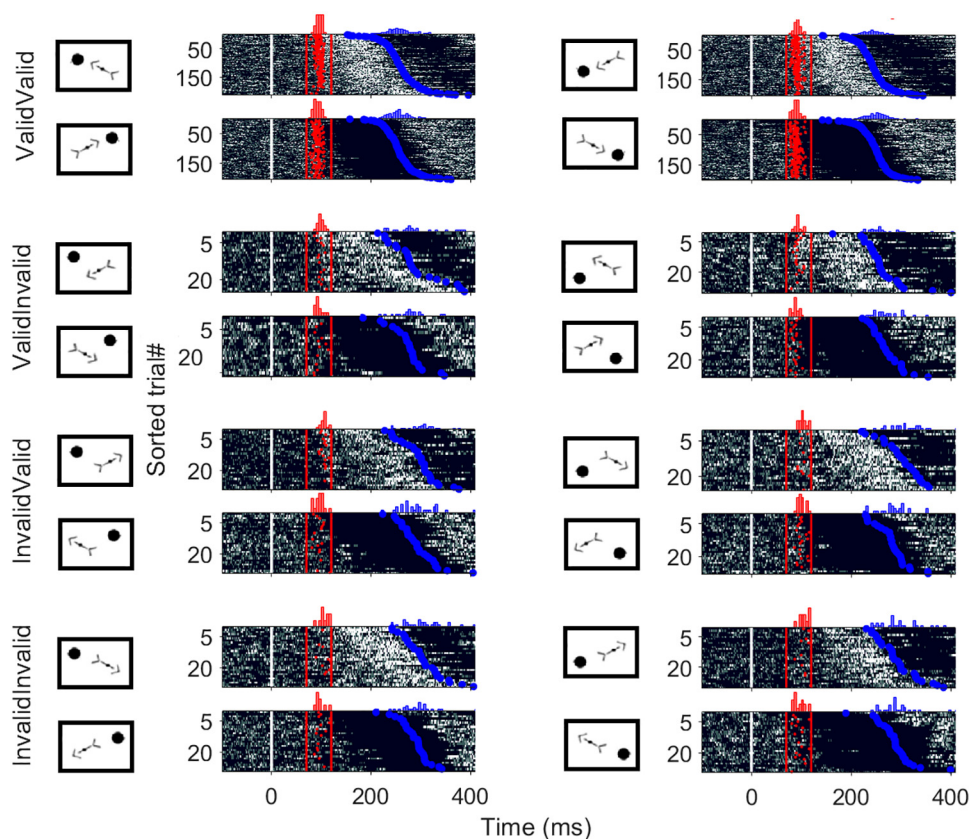
Figure 6. Surface electromyographic (EMG) activity of the pectoralis muscle (PM) muscle during the leftward and rightward movements executed toward the top (first column of panels) and bottom (second column of panels) targets of an exemplar participant who completed the first experiment and exhibited an express response in each of the four different cue conditions (see MATERIALS AND METHODS). The first line of panels shows the condition in which the target location was validly cued (i.e., Valid-Valid cue condition). The second line of panels shows the condition in which only the right/left target location was validly cued (i.e., Valid-Invalid cue condition). The third line of panels shows the condition in which only the top/bottom target location was validly cued (i.e., Invalid-Valid cue condition). The fourth line of panels shows the condition in which the target was invalidly cued (i.e., Invalid-Invalid cue condition). For each cue condition, rasters of rectified EMG activity from individual trials are shown (same format as Fig. 3, *E–H*; note that only express muscle response onset times are shown for clarity), as are the distributions of the muscle response initiation time (red histograms) and reaction time (blue histograms).

location was validly cued (i.e., Valid-Valid and Valid-Invalid cue conditions), and >100 ms when the right/left target location was invalidly cued (i.e., Invalid-Valid and Invalid-Invalid cue conditions). For both top and bottom targets, the express response initiation time in the Valid-Valid cue condition obtained via the detrended-integrated signal method was consistent with that resulting from the ROC analysis (Supplemental Fig. S1, *A* and *B*; Supplemental Table S1, *experiment 1*). For the top target, the express response magnitude was larger when the target location was validly cued (36 µV) than in the other cue conditions (Valid-Invalid 27 µV, Invalid-Valid 30 µV, Invalid-Invalid 29 µV). By contrast, for the target appearing close to the bottom of the monitor (i.e., bottom-target) the express response was 38 µV in the Valid-Invalid cue condition, 32 µV in the Valid-Valid cue condition, and ~25 µV in the Invalid-Valid and Invalid-Invalid cue conditions.

For the entire group, the prevalence of trials with an express muscle response was significantly influenced by the cue-condition ($F_{3,11}$ = 16.7, P < 0.001, η_p^2 = 0.6) and the target-location on the vertical axis ($F_{1,11}$ = 20.5, P = 0.001, η_p^2 = 0.65), and by their interaction ($F_{3,11}$ = 6.5, P = 0.001, η_p^2 = 0.37). For the top target, the SLR prevalence was significantly higher in the Valid-Valid cue condition than the other cue conditions, and significantly higher in the Valid-Invalid than Invalid-Invalid cue conditions (Fig. 7A). For the bottom target, the express response prevalence was significantly higher when the right/left target location was validly (Valid-Valid and Valid-Invalid cue conditions) than invalidly (Invalid-Valid and Invalid-Invalid cue

conditions) cued (Fig. 7D). The express response prevalence was also significantly higher for the bottom target than the top target, but only in the Valid-Invalid cue condition (Fig. 7, *A* and *D*).

The differences in express response initiation time between the cue conditions were consistent among the 12 subjects who produced an express visuomotor response and resulted in statistically significant contrasts at the single-subject level (Supplemental Fig. S2, *A* and *B*; Supplemental Table S2, *experiment 1*). The ANOVA showed a significant cue-condition main effect ($F_{3,11}$ = 103.1, P < 0.001, η_p^2 = 0.9), and a significant interaction between the cue condition and target location ($F_{3,11}$ = 3.7, P = 0.03, η_p^2 = 0.23). For both the top and bottom targets, the express response initiation time was significantly earlier when the right/left target location was validly (Valid-Valid and Valid-Invalid cue conditions) than invalidly cued (Invalid-Valid and Invalid-Invalid cue conditions; Fig. 7, *B* and *E*). The express response initiation time was also significantly shorter in the Valid-Valid cue condition than the Valid-Invalid cue condition, but only for the top target (Fig. 7B).

For the express response magnitude, we only found a significant main effect of cue condition ($F_{3,11}$ = 15.8, P < 0.001, η_p^2 = 0.6; see Fig. 7, *right*). It is worth noting, however, that the absence of a significant target-location main effect or cue-target interaction could be due to the pooling of left and right targets to compute the magnitude of express muscle responses (see MATERIALS AND METHODS). Indeed, we expected different responses from the PMch muscle to reach for the top-left and bottom-left targets. More precisely, the top-left
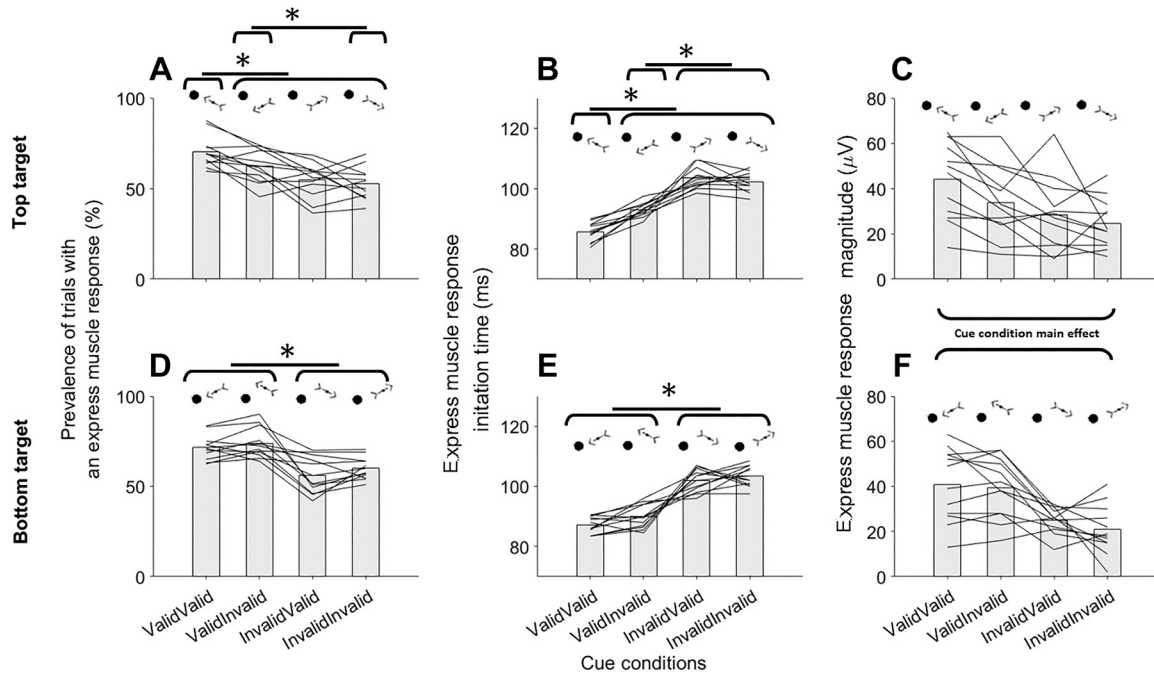
Figure 7. Express response metrics for the first experiment. Percentage of trials exhibiting an express muscle response (i.e., muscle response starting within 70–120 ms from the visual stimulus presentation; see MATERIALS AND METHODS) in the four different cue conditions for the top (*A*) and bottom (*D*) targets. Latency of the earliest stimulus-driven muscle response in the four different cue conditions for the top (*B*) and bottom (*E*) targets. Amplitude of the express visuomotor muscle response in the four different cue conditions for the top (*C*) and bottom (*F*) targets. Each black line represents one participant and the bars represent the mean across subjects. Note that the exemplar cue conditions outlined above the bars represent only top (*A–C*) and bottom (*D–F*) left target conditions for clarity. *Statistically significant differences between the cue conditions.

directed movement required a shoulder flexion in both the transverse and sagittal planes for which the PMch is primarily involved (30). By contrast, the bottom-directed reach required a shoulder transverse plane flexion and sagittal plane extension that mainly involves the sternal pectoralis fibers (30). We therefore tested if the cue-induced modulation of express responses was sensitive to the cued reaching direction, rather than the cue validity (Fig. 8). Specifically, we ran a two-way repeated-measures ANOVA analysis, with Bonferroni correction, on the express response magnitude to the left targets only in the Valid-Valid and Valid-Invalid cue conditions (within-participant factors: cue-orientation, top vs. bottom; target-cue compatibility, compatible vs. incompatible). We found statistically significant main effects for both the cue-orientation ($F_{1,11} = 9.9$, $P = 0.009$, $\eta_p^2 = 0.47$) and target-cue compatibility ($F_{1,11} = 10.6$, $P = 0.008$, $\eta_p^2 = 0.49$). For both compatible and incompatible target-cue conditions, express muscle responses were significantly larger for the top than bottom cue orientation (Fig. 8). The fact that the biomechanical action of the PMch aligns with the top-left target to a greater extent than the bottom-left target suggests that overt cue-driven expectation primes circuits that are sufficiently along the sensory to motor continuum to reflect biomechanical details of expected movement. For both cue orientations, the express response was significantly larger when the target location was compatible than incompatible with the cue orientation (Fig. 8). This suggests that matching prior motor signals with spatially compatible visual inputs facilitated the generation of larger express visuomotor muscle responses.

Experiment 2

Task correctness and reaction time.

The proportion of correct reaches was significantly influenced by the cue (cue-condition main effect: $F_{3,15} = 20.02$, $P < 0.001$, $\eta_p^2 = 0.57$). For both the top and bottom targets, the proportion of correct reaches was significantly higher
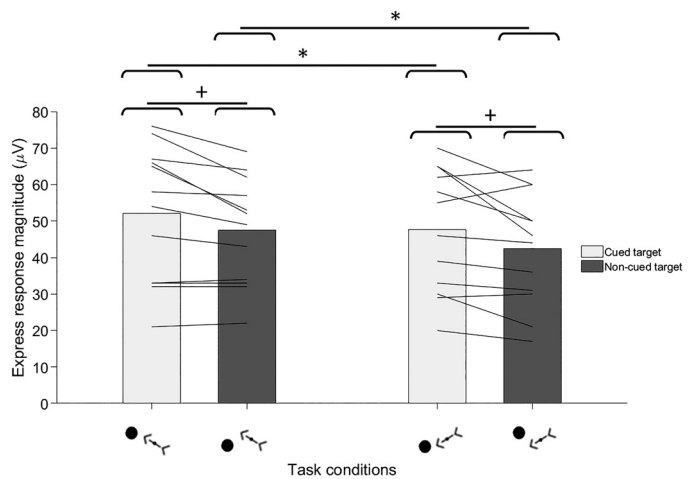

Figure 8. Dependency of the magnitude of express muscle response to the left targets on the cue orientation and its compatibility with the target location. Each black line represents one of the twelve subjects of the first experiment who exhibited an express response and the bars represent the mean across subjects. *Statistically significant differences between the cue orientation conditions; +Statistically significant differences between the cue-target compatibility conditions.
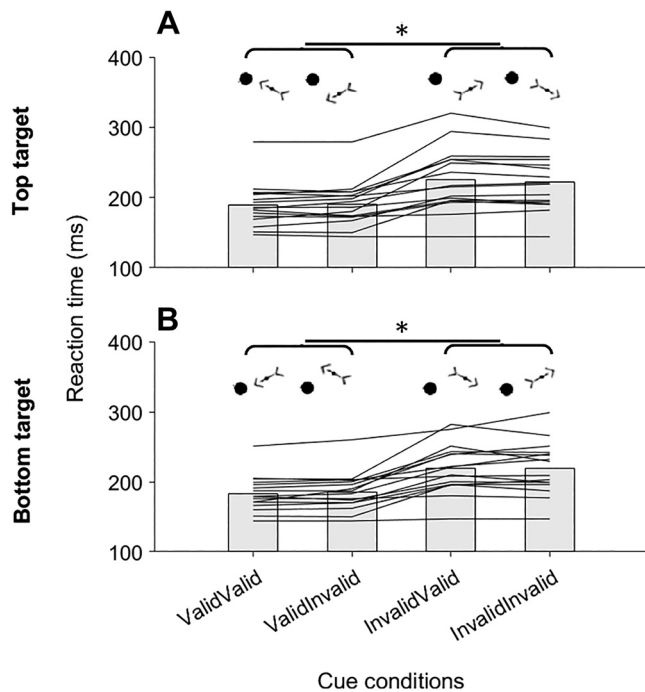
Figure 9. Reaction time of correct reaches in the four different cue conditions (see Fig. 1*A*) for the top (*A*) and bottom (*B*) targets of the second experiment. Each black line represents one participant and the bars represent the mean across subjects. Note that the exemplar cue conditions outlined above the bars represent only top (*A*) and bottom (*B*) left target conditions for clarity. *Statistically significant differences between the cue conditions.

when the reaching direction was validly cued than invalidly cued (Table 1). By contrast, the proportion of correct responses was not influenced by the top/bottom cue validity. These results suggest that the initial movement direction was biased solely by the right/left cue orientation.

The RT was significantly influenced by the cue validity (cue-condition main effect: $F_{3,15} = 36.6$, $P < 0.001$, $\eta_p^2 = 0.71$). For both the top and bottom targets, the RT was significantly shorter when the reaching direction was validly (Valid-Valid and Valid-Invalid cue conditions) than invalidly (Invalid-Valid and Invalid-Invalid cue conditions) cued (Fig. 9). This indicates that the participants used the right/left cue orientation to improve their performance, regardless of the top/bottom cue validity.

Express muscle response.

Eleven of the 16 participants (i.e., ~69%) in the second experiment exhibited an express visuomotor response on the PMch muscle on each of the four cue conditions. Again, no participant consistently exhibited a PD muscle express response across the different cue conditions and, thereby, only the express responses recorded on the PMch muscle were considered for statistical analysis.

Figure 10 shows the EMG recordings from one of the 11 subjects who showed an express response on the PMch muscle for each cue condition of the first experiment. The percentage of trials with an express muscle response was larger when the reaching direction was validly (Valid-Valid cue condition: top target 89%, bottom target 87%; Valid-

Invalid cue condition: top target 84%, bottom target: 91%) than invalidly cued (Invalid-Valid cue condition: top target 36%, bottom target 57%; Invalid-Invalid cue condition: top target 52%, bottom target 48%). For both the top and bottom targets, the earliest target-driven muscle response was ~93 ms when the reaching direction was validly cued (i.e., Valid-Valid and Valid-Invalid cue conditions), and at ~106 ms when it was invalidly cued (i.e., Invalid-Valid and Invalid-Invalid cue conditions; see MATERIALS AND METHODS).

Similar results were found among the 11 positive SLR subjects of the second experiment (Supplemental Fig. S2, *C* and *D* and Supplemental Table S2, *experiment 2*). Again, the express response initiation times in the Valid-Valid cue condition were consistent among the detrended-integrated and ROC methods (Supplemental Fig. S1, *C* and *D*; Supplementary Table S1, *experiment 2*). The express response magnitude was larger when the reaching direction was validly (Valid-Valid cue condition: top target 108 µV, bottom target: 127 µV; Valid-Invalid cue condition: top target 114 µV, bottom target: 114 µV) than invalidly cued (Invalid-Valid cue condition: top target: 70 µV, bottom target: 58 µV; Invalid-Invalid cue condition: top target 51 µV, bottom target 77 µV).

For the entire group, the three express responses metrics were significantly influenced by the cue conditions (prevalence: $F_{3,10} = 15.82$, $P < 0.001$, $\eta_p^2 = 0.61$; initiation time: $F_{3,10} = 159.79$, $P < 0.001$, $\eta_p^2 = 0.94$; magnitude: $F_{3,10} = 11.13$, $P < 0.001$, $\eta_p^2 = 0.53$). For both the top and bottom targets, the express response prevalence and magnitude were significantly larger, and the express response initiation time was significantly earlier, when the reaching direction was validly than invalidly cued (Fig. 11). These findings indicate that validly cueing the reaching direction positively modulated the express visuomotor behavior, regardless of the prior information about the probable target location in the vertical axis.

DISCUSSION

Across the two experiments, we characterized cue-induced modulations of express arm muscle responses and long-latency kinematic parameters during a target-directed reaching task. Akin to express saccades (20, 21), express arm muscle responses result from rapid sensorimotor transformations of visual inputs into motor outputs. Furthermore, express muscle responses appear to lack the flexibility to implement task rules as they consistently encode the physical location of visual targets within ~100 ms from their presentation even in anti-reach (7) or no-reach (10) tasks. This implies a control network with properties similar to that for express saccades, which involves the midbrain superior colliculus and the brainstem reticular formation (31, 32). Considering that the participants had to interpret symbolic meanings of cue orientations, our results suggest that even the earliest neural computations required to transform visual inputs into motor outputs are sensitive to modulation reflecting top-down expectations. Notably, the time for sensory-to-motor transformation of visual inputs along the express pathway was ~15 ms shorter with valid than invalid cues.
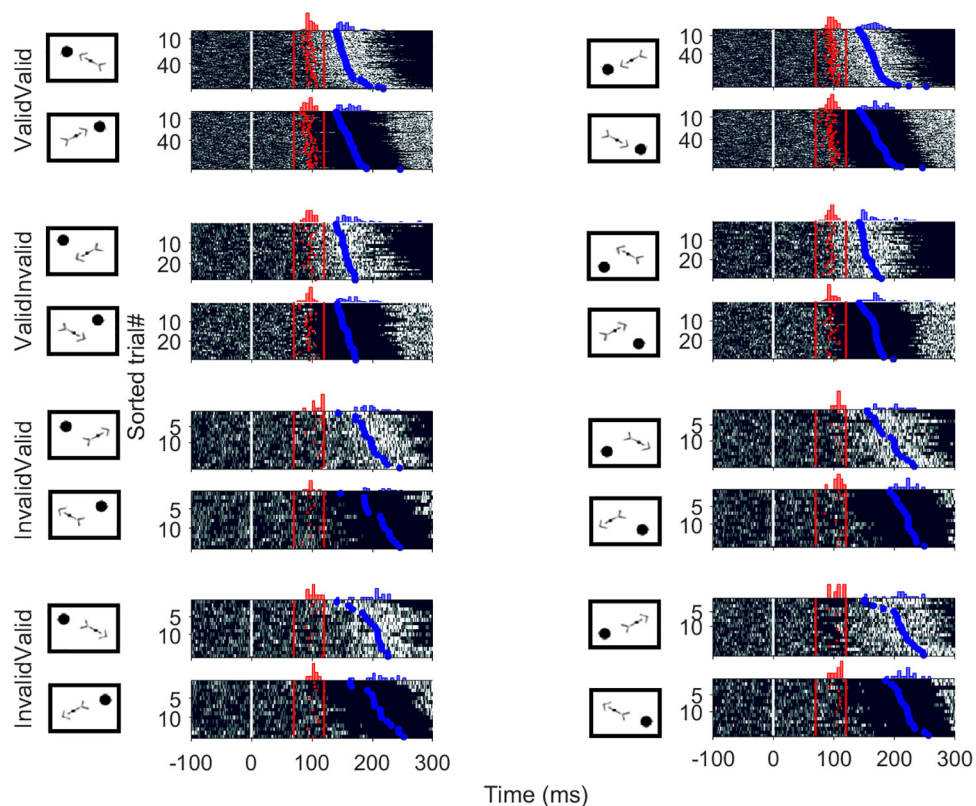
Figure 10. Surface electromyographic (EMG) activity of the pectoralis muscle (PM) muscle during the leftward and rightward movements executed toward the top and bottom targets of an exemplar participant who completed the second experiment and exhibited an express response in each of the four different cue conditions (same format as Fig. 6).

Cue-Driven Visuospatial Facilitation

In the first experiment in which the participants could execute four distinct target-directed reaches, validly cueing the target location facilitated express visuomotor behavior relative to the invalid cue conditions. This could reflect an overt cue-induced mechanism for orienting attention (33) or an attentional bias driven by motor intention, a phenomenon known as the intentional weighting mechanism (34–36). Attention deployment toward the expected (cued) target location would facilitate and inhibit the sensory-to-motor transformation of validly and invalidly cued visual inputs, respectively. Notably, there are extensive corticotectal projections that are well-placed to mediate the top-down delivery of cortical (e.g., cue-driven) signals to the superior colliculus (37, 38), and modulate the sensorimotor transformations operated by this midbrain structure. This is consistent with evidence of reduced collicular activity (39) and express saccade prevalence after cryogenic inactivation of the frontal eye field in monkeys (40). Earlier behavioral work also showed that express visuomotor behavior is modulated as a function of temporal and spatial stimulus predictability (16, 17, 20, 41), and explicit cue-driven instructions (42). Overtly cueing the target location might facilitate visuospatial processing of stimuli at the cued locations on the collicular visual map such that the visual signals encoding expected targets could be more rapidly integrated within visuomotor circuits that project to the motor nuclei of the reticular formation (for a review see Ref. 19).

Although the target appeared at each of the three invalidly cued locations with equal probability in the first experiment, express muscle responses were facilitated for the Valid-Invalid cue condition relative to the other invalid cue conditions. This might reflect a broadly distributed facilitation of the colliculus encoding the cued right/left visual hemi field, possibly by reducing excitatory drive to the foveal fixation zone that has nonspecific inhibitory projections to all extrafoveal parts of that colliculus (for review see Refs. 19 and 37). Basso and Wurtz (43), however, showed that validly cueing one of eight possible targets (45° between the targets; ~10 dva of eccentricity from fixation) facilitated only the collicular neurons encoding the cued locus. Some facilitation of collicular visual map restricted at the cued locus should have occurred also in our task because we used an even larger (60°) top-bottom target gap. Furthermore, the cue-induced modulations of express muscle response were not symmetrical around the horizontal axis. Specifically, providing only right/left valid information (i.e., Valid-Invalid cue condition) impaired express muscle responses to the top targets, but not bottom targets, relative to valid cue conditions (i.e., Valid-Valid cue condition). This asymmetry argues against a generalized cue-driven left/right hemifield enhancement of attention.

Cue-Driven Motor Facilitation

Larger express muscle responses resulted from validly cueing the location of top-left than bottom-left targets (see first and third bars in Fig. 8) of the first experiment. Although this could reflect functional discontinuity of the superior colliculus across the horizontal axis (44), our results for invalid top/bottom cue conditions suggest a
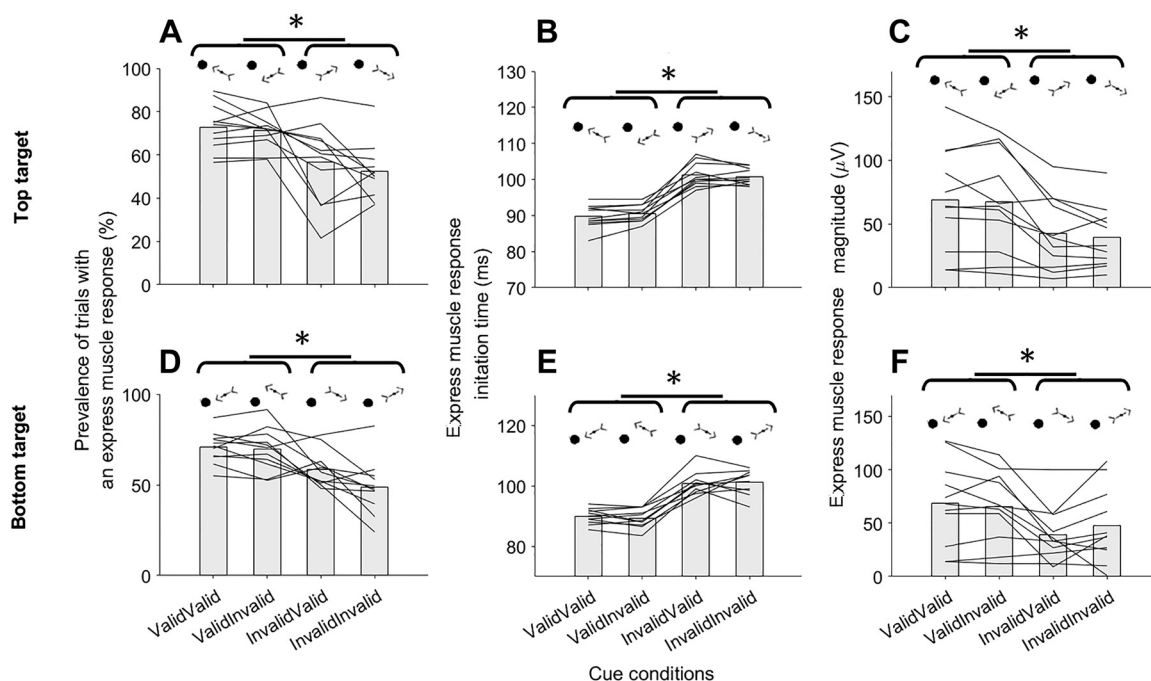
Figure 11. Express response metrics in the four different cue conditions for the *top* (first row of panels) and *bottom* (second row of panels) targets of the second experiment (same format as Fig. 7). *A* and *D* show the percentage of trials exhibiting an express muscle response. *B* and *E* show the latency of the earliest stimulus-driven muscle response. *C* and *F* show the amplitude of the express visuomotor muscle response. *Statistically significant differences between the cue conditions.

different mechanism. Specifically, larger express muscle responses were detected by invalidly cueing the bottom-left (i.e., cue oriented top-left) than top-left (i.e., cue oriented bottom-left) target (see second and fourth bars in Fig. 8). Notably, this is in line with the mechanical output required to the PMch to bring the hand at top and bottom target locations (see RESULTS).

The pectoralis major muscle has multiple zones of innervations that are confined medially within the cranio-caudal muscle length (45). This subserves discrete recruitment of different muscle portions to accomplish the required movement depending on the posture and the upper limb osteo-kinematics (46–48). Critically, the compatibility between express muscle responses and cued reaching directions suggests that the cue-induced modulations of express muscle responses were inclusive of prior cue-driven motor signals, rather than solely sensitive to facilitation of rapid visuospatial target processing.

The cue-induced motor preparation mechanism was further tested in the second experiment in which a single rightward or leftward reach was required. Here, validly cueing the right/left component of the target location facilitated express muscle response to both the top and bottom targets to a similar degree, irrespective of the top/bottom cue validity. Again, this is not consistent with evidence of collicular functional asymmetry across the horizontal axis (44), but rather appears to reflect a mechanism by which a prepared (i.e., cued) motor response can be rapidly released by any stimulus appearing compatibly with the expected reaching direction. By contrast, express muscle responses were likely impaired in invalid right/left cue conditions because of additional neural computations required to invert the agonist/

antagonist muscle contribution to the prepared motor plans within the putative subcortical express pathway. Notably, our results are consistent with previous work by Gu et al. (8) in which straight target-directed reaches were encumbered by virtual obstacles that were presented one second before the target, thus prompting pretarget preparation of curvilinear reaches. The magnitude of express muscle response was similar for targets requiring curved reaching trajectories (e.g., right-then-top) and for those presented in line with the initial phase of the planned curved movement (e.g., right), whereas incongruent targets led to weaker express arm muscle responses.

Note that a cue-induced mechanism for motor preparation is also consistent with the cue-induced modulations of RT and kinematics. In the first experiment, providing only valid horizontal cues (i.e., Valid-Invalid cue conditions) biased the initial movement trajectory toward the invalid top/bottom cued direction. This led to significant reduction in task accuracy and increase in initial trajectory angle error for the Valid-Invalid cue condition relative to the other cue conditions. Furthermore, the negative correlation observed between the trajectory angle error and the RT in the Valid-Invalid cue condition suggests a progressive shift from cue-driven to target-driven motor plans. This is consistent with evidence of time-based inhibition of nontarget-directed motor responses, such as those encoding the location of distractor stimuli. Specifically, the occurrence of distractor-directed motor responses depends on the time available to suppress the distractor-driven motor signals (for review see Ref. 49). The large initial trajectory angle errors in the Valid-Invalid cue conditions might, therefore, reflect under-inhibited motor plans to reach the invalid top/bottom cued

location due to short delay between target presentation and movement initiation. This may reflect a situation in which a response is initiated as soon as the compatibility between prestimulus and poststimulus motor plans is good enough to achieve the task goal, consistent with a tradeoff between rapid versus efficient (shorter trajectories → lower energetic costs) responses. By contrast, the long RTs recorded in the invalid right/left cue conditions could reflect additional neural computations to transform the visual stimuli into unprepared motor signals and inhibit the cue-driven motor plans to avoid wrong movements. The results of the second experiment are also consistent with a cue-induced mechanism for motor preparation, since reaches were facilitated (inhibited) for any visual input compatible (incompatible) with the cued reach direction, regardless of cue-driven sensory expectations.

Classical work involving single unit brain recordings from monkeys indicated that multiple potential target directions are represented simultaneously in premotor cortices (50) and the superior colliculus (43). In contexts of target location uncertainty (e.g., go-before-you-know tasks; 51), these parallel motor representations have been proposed to be averaged such that the initial movement is directed midway between the possible target locations [motor averaging hypothesis (51)]. More recent evidence from simultaneous recordings of multiple units in premotor cortex (49), however, suggests that the brain prepares a single contextually relevant motor plan at a time that can be modified online to address the actual target location [performance optimization hypothesis (51)]. Notably, the cortical areas involved in pretarget motor planning are mutually interconnected with those encoding quantity, probability, and value information (52, 53) that can facilitate the decision of which movement to prepare. In our experiments, cueing the probable target location could trigger a neural mechanism by which a single cue-driven motor plan was prepared and then integrated with posttarget motor signals to produce the final motor output (54, 55). Indeed, the cue-induced modulations of express muscle responses were consistent with the biomechanical requirements for moving the arm toward the cued locations, rather than midway between the cued and actual target locations (see the first vs. third and second vs. fourth bar contrasts in Fig. 8). By contrast, the reduced magnitude of express muscle responses in invalid top/bottom cue conditions relative to valid cues (see the first vs. second and third vs. fourth bar contrasts in Fig. 8) could reflect the neural cost to integrate pretarget (cue-driven) with posttarget (target-driven) motor plans along the putative subcortical express pathway. Note, however, that although our results seem consistent with the performance optimization hypothesis (51), they cannot confirm that the brain prepares a single motor plan at time in contexts of target uncertainty as we cued the probable target location. It is also worth noting that the pattern of results across the different cue conditions could be influenced by the specific attributes of our paradigm, such as the shorter between-target distance on the vertical than horizontal axes (see MATERIALS AND METHODS).

The cortical signals affording cue-induced motor expectations might set the collicular visuomotor state (43) via the corticotectal projections (37, 38, 56), thus modulating the neural computations to integrate cue-driven and target-driven motor plans operated by this midbrain structure.

Downstream from the superior colliculus, the brainstem reticular formation receives extensive descending projections from the cortical motor areas. Keizer and Kuypers (57, 58) showed direct corticoreticular projection originating from primary motor and premotor cortices in cats and monkeys. More recent studies extended this knowledge by showing both ipsilateral and contralateral corticoreticular projections from the primary motor cortex (59, 60), the supplementary motor area (59–61), and the premotor cortex (59, 60) to the motor nuclei of the reticular formation. These corticoreticulo projections might subserve the top-down delivery of preparatory motor signals and modulate the reticular formation motor set before the stimulus presentation. Overall, our findings are consistent with existing ideas about the role of the reticular formation in the rapid release of prepared motor actions (62, 63) at the arrival of triggering signals (e.g., from the superior colliculus) that arise from the presentation of salient stimuli.

Functional Motor Behavior Implications of Express Muscle Responses

It is worth nothing that the earliest volitional visuomotor behavior appears to be facilitated by express muscle responses. We and others previously showed that larger express muscle responses were associated with earlier mechanical responses in humans (5, 7, 16, 17). Furthermore, Gu et al. (7) recorded express (∼110 ms) hand-force divergences encoding the target location whose amplitude correlated with that of express muscle responses. Critically, the initiation time of hand-force divergence is consistent with a ∼30 ms electromechanical delay (64) from the earliest stimulus-driven muscle response. Therefore, even though express muscle responses may not by themselves produce enough muscle force to reach the threshold for RT detection, they will still alter the muscle mechanical state to facilitate the subsequent volitional train of action potentials from spinal motoneurons.

Conclusions

The present work documents modulations of express visuomotor arm muscle responses due to explicit cue-driven information in humans. The modulations of express responses appear to reflect a cue-driven mechanism for motor preparation within the putative subcortical express pathway, potentially including the midbrain superior colliculus and brainstem reticular formation. This might subserve the rapid and robust release of prepared motor responses to predictable visual events. Overall, our data lend support to the idea that there are meaningful subcortical contributions to visually guided arm functions in humans, and that putative subcortical express pathway is subject to cortical modulation that enhances behavioral flexibility.

SUPPLEMENTAL DATA

Supplemental Figs. S1 and S2 and Tables S1 and S2: https://doi.org/10.17605/OSF.IO/75JT2.

GRANTS

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

REFERENCES

1. **Haith AM**, **Huberdeau DM**, **Krakauer JW.** Hedging your bets: intermediate movements as optimal behavior in the context of an incomplete decision. *PLoS Comput Biol* 11: e1004171, 2015. doi:10.1371/journal.pcbi.1004171.

2. **Luce RD.** *Response Times: Their Role in Inferring Elementary Mental Organization.* New York: Oxford University Press, 1986.

3. **Smeets JB**, **Oostwoud Wijdenes L**, **Brenner E.** Movement adjustments have short latencies because there is no need to detect anything. *Motor Control* 20: 137–148, 2016. doi:10.1123/mc.2014-0064.

4. **Wong AL**, **Haith AM**, **Krakauer JW.** Motor planning. *Neuroscientist* 21: 385–398, 2015. doi:10.1177/1073858414541484.

5. **Pruszynski AJ**, **King GL**, **Boisse L**, **Scott SH**, **Flanagan RJ**, **Munoz DP.** Stimulus-locked responses on human arm muscles reveal a rapid neural pathway linking visual input to arm motor output. *Eur J Neurosci* 32: 1049–1057, 2010. doi:10.1111/j.1460-9568.2010.07380.x.

6. **Wood DK**, **Gu C**, **Corneil BD**, **Gribble PL**, **Goodale MA.** Transient visual responses reset the phase of low-frequency oscillations in the skeletomotor periphery. *Eur J Neurosci* 42: 1919–1932, 2015. doi:10.1111/ejn.12976.

7. **Gu C**, **Wood DK**, **Gribble PL**, **Corneil BD.** A trial-by-trial window into sensorimotor transformations in the human motor periphery. *J Neurosci* 36: 8273–8282, 2016. doi:10.1523/JNEUROSCI.0899-16.2016.

8. **Gu C**, **Pruszynski JA**, **Gribble PL**, **Corneil BD.** Done in 100 ms: path-dependent visuomotor transformation in the human upper limb. *J Neurophysiol* 119: 1319–1328, 2018. doi:10.1152/jn.00839.2017.

9. **Gu C**, **Pruszynski JA**, **Gribble PL**, **Corneil BD.** A rapid visuomotor response on the human upper limb is selectively influenced by implicit motor learning. *J Neurophysiol.* 121: 85–95, 2019. doi:10.1152/jn.00720.2018.

10. **Atsma J**, **Maij F**, **Gu C**, **Medendorp WP**, **Corneil BD.** Active braking of whole-arm reaching movements provides single-trial neuromuscular measures of movement cancellation. *J Neurosci* 38: 4367–4382, 2018. doi:10.1523/JNEUROSCI.1745-17.2018.

11. **Kozak RA**, **Kreyenmeier P**, **Gu C**, **Johnston K**, **Corneil BD.** Stimulus-locked responses on human upper limb muscles and corrective reaches are preferentially evoked by low spatial frequencies. *eNeuro* 6: ENEURO.0301-19.2019, 2019. doi:10.1523/ENEURO.0301-19.2019.

12. **Glover IS**, **Baker SN.** Modulation of rapid visual responses during reaching by multimodal stimuli. *J Neurophysiol* 122: 1894–1908, 2019. doi:10.1152/jn.00158.2019.

13. **Selen LPJ**, **Corneil BD**, **Medendorp WP.** Single-trial dynamics of competing reach plans in the human motor periphery (Preprint). *bioRxiv* 765180, 2021. doi:10.1101/765180.

14. **Kozak AR**, **Cecala AL**, **Corneil BD.** An emerging target paradigm evokes fast visuomotor responses on human upper limb muscles. *J Vis Exp* e61428, 2020. doi:10.3791/61428.

15. **Kozak AR**, **Corneil BD.** High contrast, moving targets in an emerging target paradigm promote fast visuomotor responses during visually guided reaching. *J Neurophysiol* 126: 68–81, 2021. doi:10.1152/jn.00057.2021.

16. **Contemori S**, **Loeb GE**, **Corneil BD**, **Wallis G**, **Carroll TJ.** The influence of temporal predictability on express visuomotor responses. *J Neurophysiol* 125: 731–747, 2021. doi:10.1152/jn.00521.2020.

17. **Contemori S**, **Loeb GE**, **Corneil BD**, **Wallis G**, **Carroll TJ.** Trial-by-trial modulation of express visuomotor responses induced by symbolic or barely detectable cues. *J Neurophysiol* 126: 1507–1523, 2021. doi:10.1152/jn.00053.2021.

18. **Kearsley SL**, **Cecala AL**, **Kozak RA**, **Corneil BD.** Express arm responses appear bilaterally on upper-limb muscles in an arm choice reaching task. *J Neurophysiol* 127: 969–983, 2022. doi:10.1152/jn.00494.2021.

19. **Corneil BD**, **Munoz DP.** Overt responses during covert orienting. *Neuron* 82: 1230–1243, 2014. doi:10.1016/j.neuron.2014.05.040.

20. **Pare M**, **Munoz DP.** Saccadic reaction time in the monkey: advanced preparation of oculomotor programs is primarily responsible for express saccade occurrence. *J Neurophysiol* 76: 3666–3681, 1996. doi:10.1152/jn.1996.76.6.3666.

21. **Fischer B**, **Boch R.** Saccadic eye-movements after extremely short reaction-times in the monkey. *Brain Res* 260: 21–26, 1983. doi:10.1016/0006-8993(83)90760-6.

22. **Edelman JA**, **Keller EL.** Activity of visuomotor burst neurons in the superior colliculus accompanying express saccades. *J Neurophysiol* 76: 908–926, 1996. doi:10.1152/jn.1996.76.2.908.

23. **Dorris MC**, **Paré M**, **Munoz DP.** Neuronal activity in monkey superior colliculus related to the initiation of saccadic eye movements. *J Neurosci* 17: 8566–8579, 1997. doi:10.1523/JNEUROSCI.17-21-08566.1997.

24. **Schiller PH**, **Sandell JH**, **Maunsell JH.** The effect of frontal eye field and superior colliculus lesions on saccadic latencies in the rhesus monkey. *J Neurophysiol* 57: 1033–1049, 1987. doi:10.1152/jn.1987.57.4.1033.

25. **Howard S**, **Ingram JN**, **Wolpert DM.** A modular planar robotic manipulandum with end-point torque control. *J Neurosci Methods* 181: 199–211, 2009. doi:10.1016/j.jneumeth.2009.05.005.

26. **Brainard DH.** The Psychophysics toolbox. *Spat Vis* 10: 433–436, 1997.

27. **Pelli DG.** The VideoToolbox software for visual psychophysics: transforming numbers into movies. *Spat Vis* 10: 437–442, 1997.

28. **Haith AM**, **Pakpoor J**, **Krakauer JW.** Independence of movement preparation and movement initiation. *J Neurosci* 36: 3007–3015, 2016. doi:10.1523/JNEUROSCI.3245-15.2016.

29. **Cross KP**, **Cluff T**, **Takei T**, **Scott SH.** Visual feedback processing of the limb involves two distinct phases. *J Neurosci* 39: 6751–6765, 2019. doi:10.1523/JNEUROSCI.3112-18.2019.

30. **Neumann DA.** *Kinesiology of the Musculoskeletal System: Foundations for Rehabilitation* (3rd ed.). St. Louis, MO: Mosby, 2016, p. 160–161.

31. **Corneil BD**, **Olivier E**, **Munoz DP.** Visual responses on neck muscles reveal selective gating that prevents express saccades. *Neuron* 42: 831–841, 2004. doi:10.1016/s0896-6273(04)00267-3.

32. **Corneil BD**, **Munoz DP**, **Chapman BB**, **Admans T**, **Cushing SL.** Neuromuscular consequences of reflexive covert orienting. *Nat Neurosci* 11: 13–15, 2008. doi:10.1038/nn2023.

33. **Posner MI.** Orienting of attention: then and now. *Q J Exp Psychol (Hove)* 69: 1864–1875, 2016. doi:10.1080/17470218.2014.937446.

34. **Wykowska A**, **Schubö A**, **Hommel B.** How you move is what you see: action planning biases selection in visual search. *J Exp Psychol Hum Percept Perform* 35: 1755–1769, 2009. doi:10.1037/a0016798.

35. **Wykowska A**, **Schubo A.** Action intentions modulate allocation of visual attention: electrophysiological evidence. *Front Psychol* 3: 379, 2012. doi:10.3389/fpsyg.2012.00379.

36. **Hommel B.** Grounding attention in action control: the intentional control of selection. In: *A New Perspective in the Cognitive Science of Attention and Action: Effortless Attention*, edited by Bruya B. Cambridge, MA: MIT Press, 2010, p. 121–140.

37. **Baluch F**, **Itti L.** Mechanisms of top-down attention. *Trends Neurosci* 34: 210–224, 2011. doi:10.1016/j.tins.2011.02.003.

38. **Knudsen EI.** Neural circuits that mediate selective attention: a comparative perspective. *Trends Neurosci* 41: 789–805, 2018. doi:10.1016/j.tins.2018.06.006.

39. **Peel TR**, **Dash S**, **Lomber SG**, **Corneil BD.** Frontal eye field inactivation diminishes superior colliculus activity, but delayed saccadic accumulation governs reaction time increases. *J Neurosci* 37: 11715–11730, 2017. doi:10.1523/JNEUROSCI.2664-17.2017.

40. **Dash S**, **Peel TR**, **Lomber SG**, **Corneil BD.** Frontal eye field inactivation reduces saccade preparation in the superior colliculus but does not alter how preparatory activity relates to saccades of a given latency. *eNeuro* 5: ENEURO.0024-18.2018, 2018. doi:10.1523/ENEURO.0024-18.2018.

41. **Dorris MC**, **Olivier E**, **Munoz DP.** Competitive integration of visual and preparatory signals in the superior colliculus during saccadic programming. *J Neurosci* 27: 5053–5062, 2007. doi:10.1523/JNEUROSCI.4212-06.2007.

42. **Edelman JA**, **Kristjánsson A**, **Nakayama K.** The influence of object-relative visuomotor set on express saccades. *J Vis* 7: 12, 2007. doi:10.1167/7.6.12.

43. **Basso MA**, **Wurtz RH.** Modulation of neuronal activity in superior colliculus by changes in target probability. *J Neurosci* 18: 7519–7534, 1998. doi:10.1523/JNEUROSCI.18-18-07519.1998.

44. **Hafed ZM**, **Chen C-Y.** Sharper, stronger, faster upper visual field representation in primate superior colliculus. *Curr Biol* 26: 1647–1658, 2016. doi:10.1016/j.cub.2016.04.059.

45. **Mancebo FD**, **Cabral HV**, **de Souza LML**, **de Oliveira LF**, **Vieira TM.** Innervation zone locations distribute medially within the pectoralis major muscle during bench press exercise. *J Electromyogr Kinesiol* 46: 8–13, 2019. doi:10.1016/j.jelekin.2019.03.002.

46. **Trebs AA**, **Brandenburg JP**, **Pitney WA.** An electromyography analysis of 3 muscles surrounding the shoulder joint during the performance of a chest press exercise at several angles. *J Strength Cond Res* 24: 1925–1930, 2010. doi:10.1519/JSC.0b013e3181ddfae7.

47. **Mancebo FD**, **Cabral HV**, **De Souza LML**, **Oliveira LF.** Is the EMGs amplitude distribution spatially localizes in the pectoralis major muscle during the inclined bench press? In: *XXVI Brazilian Congress on Biomedical Engineering*, edited by Costa-Felix R, Machado J, Alvarenga A. Singapore: Springer, 2019, vol. 70, p. 299–303.

48. **Lee H.** Force direction and arm position affect contribution of clavicular and sternal parts of pectoralis major muscle during muscle strength testing. *Hand Ther* 32: 71–79, 2019. doi:10.1016/j.jht.2017.08.007.

49. **Dekleva BM**, **Kording KP**, **Miller LE.** Single reach plans in dorsal premotor cortex during a two-target task. *Nat Commun* 9: 3556, 2018. doi:10.1038/s41467-018-05959-y.

50. **Cisek P**, **Kalaska JF.** Neural correlates of reaching decisions in dorsal premotor cortex: Specification of multiple direction choices and final selection of action. *Neuron* 3: 801–814, 2005. doi:10.1016/j.neuron.2005.01.027.

51. **Alhussein L**, **Smith MA.** Motor planning under uncertainty. *eLife* 10: e67019, 2021. doi:10.7554/eLife.67019.

52. **Gold JI**, **Shadlen MN.** The neural basis of decision making. *Annu Rev Neurosci* 30: 535–574, 2007. doi:10.1146/annurev.neuro.29.051605.113038.

53. **Hubbard EM**, **Piazza M**, **Pinel P**, **Dehaene S.** Interactions between number and space in parietal cortex. *Nat Rev Neurosci* 6: 435–448, 2005. doi:10.1038/nrn1684.

54. **Hunt LT**, **Dolan RJ**, **Behrens TEJ.** Hierarchical competitions subserving multi-attribute choice. *Nat Neurosci* 17: 1613–1622, 2014. doi:10.1038/nn.3836.

55. **Hunt LT**, **Hayden BY.** A distributed, hierarchical and recurrent framework for reward-based choice. *Nat Rev Neurosci* 18: 172–182, 2017. doi:10.1038/nrn.2017.7.

56. **Boehnke SE**, **Munoz DP.** On the importance of the transient visual response in the superior colliculus. *Curr Opin Neurobiol* 18: 544–551, 2008. doi:10.1016/j.conb.2008.11.004.

57. **Keizer K**, **Kuypers HGJM.** Distribution of corticospinal neurons with collaterals to lower brain stem reticular formation in cat. *Exp Brain Res* 54: 107–120, 1984. doi:10.1007/BF00235823.

58. **Keizer K**, **Kuypers HGJM.** Distribution of corticospinal neurons with collaterals to the lower brain stem reticular formation in monkey (Macaca fascicularis). *Exp Brain Res* 74: 311–318, 1989. doi:10.1007/BF00248864.

59. **Fregosi M**, **Contestabile A**, **Hamadjida A**, **Rouiller EM.** Corticobulbar projections from distinct motor cortical areas to the reticular formation in macaque monkeys. *Eur J Neurosci* 45: 1379–1395, 2017. doi:10.1111/ejn.13576.

60. **Fisher KM**, **Zaaimi B**, **Edgley SA**, **Baker SN.** Extensive cortical convergence to primate reticulospinal pathways. *J Neurosci* 41: 1005–1018, 2021. doi:10.1523/JNEUROSCI.1379-20.2020.

61. **Darling WG**, **Ge J**, **Stilwell-Morecraft KS**, **Rotella DL**, **Pizzimenti MA**, **Morecraft RJ.** Hand motor recovery following extensive fronto-parietal cortical injury is accompanied by upregulated corticoreticular projections in monkey. *J Neurosci* 38: 6323–6339, 2018. doi:10.1523/JNEUROSCI.0403-18.2018.

62. **Marinovic W**, **Tresilian JR.** Triggering prepared actions by sudden sounds: reassessing the evidence for a single mechanism. *Acta Physiol (Oxf)* 217: 13–32, 2016. doi:10.1111/apha.12627.

63. **Carlsen AN**, **Maslovat D.** Startle and the StartReact effect: physiological mechanisms. *J Clin Neurophysiol* 36: 452–459, 2019. doi:10.1097/WNP.0000000000000582.

64. **Norman RW**, **Komi PV.** Electromechanical delay in skeletal muscle under normal movement conditions. *Acta Physiol Scand* 106: 241–248, 1979. doi:10.1111/j.1748-1716.1979.tb06394.x.