*J Neurophysiol* 112: 1256–1266, 2014.
First published June 4, 2014; doi:10.1152/jn.00147.2014.

# Rapid prediction of biomechanical costs during action decisions

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Submitted 20 February 2014; accepted in final form 30 May 2014

**Cos I, Duque J, Cisek P.** Rapid prediction of biomechanical costs during action decisions. *J Neurophysiol* 112: 1256–1266, 2014. First published June 4, 2014; doi:10.1152/jn.00147.2014.—When given a choice between actions that yield the same reward, we tend to prefer the one that requires the least effort. Recent studies have shown that humans are remarkably accurate at evaluating the effort of potential reaching actions and can predict the subtle energetic demand caused by the nonisotropic biomechanical properties of the arm. In the present study, we investigated the time course over which such information is computed and comes to influence decisions. Two independent approaches were used. First, subjects performed a reach decision task in which the time interval for deciding between two candidate reaching actions was varied from 200 to 800 ms. Second, we measured motor-evoked potential (MEPs) to single-pulse transcranial magnetic stimulation (TMS) over the primary motor cortex (M1) to probe the evolving decision at different times after stimulus presentation. Both studies yielded a consistent conclusion: that a prediction of the effort associated with candidate movements is computed very quickly and influences decisions within 200 ms after presentation of the candidate actions. Furthermore, whereas the MEPs measured 150 ms after stimulus presentation were well correlated with the choices that subjects ultimately made, later in the trial the MEP amplitudes were primarily related to the muscular requirements of the chosen movement. This suggests that corticospinal excitability (CSE) initially reflects a competition between candidate actions and later changes to reflect the processes of preparing to implement the winning action choice.

decision-making; human; motor control; motor intention; TMS

WHEN DECIDING BETWEEN ACTIONS, the brain must take into account their potential payoffs as well as execution costs. The neural mechanisms for computing payoff have been the subject of many studies, implicating the orbitofrontal and medial prefrontal cortex (Camille et al. 2011; Kennerley et al. 2011; Padoa-Schioppa 2011; Rudebeck et al. 2008) as well as frontal and parietal sensorimotor areas (Gold and Shadlen 2007; Pastor-Bernier and Cisek 2011; Platt and Glimcher 1999). However, how the brain estimates the execution costs of candidate actions has only begun to be investigated (Kennerley et al. 2011; Pasquereau and Turner 2013). In particular, the biomechanical properties of effectors strongly influence not just the manner in which movements are implemented (Dounskaia et al. 2011; Goble et al. 2007) but also which movements are selected (Cos et al. 2011). For example, a boxer often punches along directions of maximal inertia to transfer maximal energy to the hit. In contrast, directions of minimal inertia are typically used to perform movements requiring precision. Does this imply that decision-making involves regions of the brain, such as the M1 or cerebellum, which are sensitive to information about biomechanics (Evarts 1968; Kalaska et al. 1989; Thach 1978)?

When humans make free choices between reaching actions, they tend to choose the one that is easiest in a biomechanical sense (Cos et al. 2011) taking into account specific control requirements (Cos et al. 2012). Importantly, even when two candidate actions are similar in terms of their launching cost, subjects still choose the one that has a lower cost at the end of movement. This suggests that we are able to predict, before movement initiation, the biomechanical properties of the entire candidate movements and choose the one for which the total cost is lowest. But how does this prediction take place, and how much time does it require?

In the present study, we used two approaches for quantifying the time course over which reach decisions evolve. The first approach used a timed-response task (Ghez et al. 1997) to determine the time interval required for viewing the candidate movements before choices take spatial and biomechanical factors into account. The second approach consisted of measuring motor-evoked potentials (MEPs) elicited by single-pulse transcranial magnetic stimulation (TMS) of M1 to assess corticospinal excitability (CSE) at different times after stimulus presentation. CSE can be used as a probe into the subject's preparatory state (van Elswijk et al. 2007), reflecting the potential value of imminent movements (Klein-Flügge and Bestmann 2012; Klein et al. 2012) as well as choice switches in conflict situations (Michelet et al. 2010). However, because CSE also correlates with the magnitude of upcoming muscular contraction (MacKinnon and Rothwell 2000), a potential quandary is raised: How can CSE increase both with one's preference and with one's impending muscular effort if one's preference is for movements that require less effort? We predict that whereas CSE initially reflects a competition between candidate movements, once the decision is made it begins to reflect the biomechanical requirements of the action that is chosen.

## METHODS

*Participants.* Eight right-handed subjects (7 women, 1 man, average age 24 yr) participated in a behavioral experiment (1 session) and a TMS experiment (2 sessions on separate days). They had no known neurological disorders and normal or corrected-to-normal vision, and they were uninformed about the purpose of these experiments. Subjects signed a consent form before participating, and the experimental protocol was approved by the Human Research Ethics Committee of the Faculty of Medicine at the University of Montreal.

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*Apparatus and task design.* The task apparatus consisted of a digitizing tablet (GTCO Calcomp, Columbia, MD; 0.915 × 0.608 m) and a half-silvered mirror suspended 16 cm above and parallel to the digitizer plane. Visual stimuli were projected onto the mirror by an LCD monitor suspended 16 cm above the mirror, producing the illusion that the targets lie on the plane of the digitizing tablet (Fig. 1*A*). Subjects made reaching movements in the horizontal plane using a digitizing stylus whose position was sampled at 125 Hz with a spatial resolution of 0.006 in. ± 0.127 mm. The control of the task, stimulus display, and synchronization of task events and signal recording were performed by a custom-written LabVIEW program (National Instruments, Austin, TX). The data were stored in a MySQL database (Oracle, Redwood Shores, CA) and analyzed using custom Matlab scripts (The MathWorks, Natick, MA).

In the behavioral session (Fig. 1*B*), subjects performed 640 trials in 4 blocks, each of which consisted of 128 two-target and 32 one-target trials. Each trial began when the subject placed the stylus in a central cyan circle (radius 1 cm) for a 300–700 ms center hold time (CHT). Next, a series of acoustic signals were systematically given at 0, 500, 1,000, and 2,000 ms after the end of CHT. Subjects were instructed to initiate movement as close as possible to the time of the fourth acoustic signal. The presentation of the visual stimuli defining the potential movements preceded that fourth signal by an observation interval of 200, 400, 600, or 800 ms, chosen pseudorandomly on each trial. In two-target trials, subjects were presented with two movement choices, each defined by a via-point (cyan dot radius 1 cm) and a target (3 × 1-cm blue rectangle) placed in one of the arrangements shown in Fig. 1*D*. In the "T1-Major" (T1M) arrangements, the movement toward the right target (T1) required less biomechanical effort than the movement toward the left target (T2), whereas the opposite was true in the "T1-minor" (T1m) arrangements. As described in detail in Cos et al. (2011), biomechanical effort was characterized using the end-point mobility ellipse (Hogan 1985a, 1985b, 1985c), which summarizes how muscle torques translate to

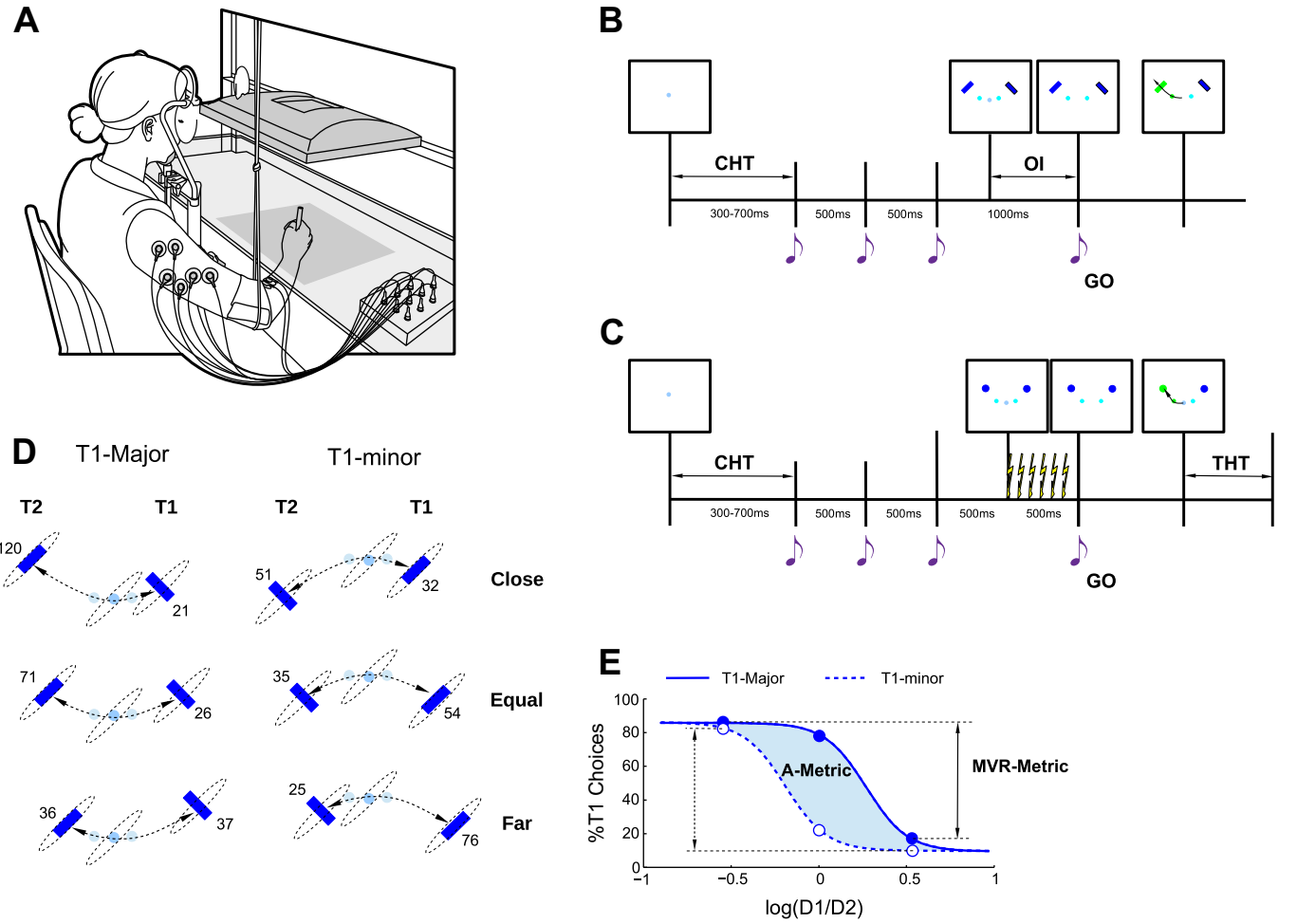


Fig. 1. *A*: task apparatus, showing a subject seated at the digitizing tablet with her head in a chin rest and holding the stylus in her right hand. *B*: description of the time course of a trial. The boxes depict the stimuli presented to subjects on a typical trial (see METHODS, *Apparatus and task design*, for further details). The pale blue dot represents the origin, the 2 cyan dots the via-points, and the 2 blue rectangles the targets. The origin disappeared when the stylus left it, and the via-point and the target turned green when the stylus slid over them. Task events in the behavioral session are center hold time (CHT) and observation interval (OI), which is 200, 400, 500, or 800 ms. *C*: description of the time course of a TMS trial (same as in *B* except that the targets are round blue circles). Lightning bolts indicate stimulation times at 1, 150, 200, 250, 300, and 350 ms after target onset. THT, target hold time. *D*: the 6 pairs of target arrangements shown to subjects during two-target trials. The starting circle and via-points are represented by cyan dots (not to scale) and the targets by 3 × 1-cm rectangles. Dotted ellipses illustrate the biomechanical mobility at the starting and target locations, and arrows demonstrate the required movement paths. Note that in the "T1-Major" (T1M) arrangements, movement to T1 arrives along the major axis of the mobility ellipse, whereas movement to T2 arrives along the minor axis. This is reversed in the "T1-minor" (T1m) arrangements. Numbers next to the targets indicate estimates of the energy required for the movement, in mJ. *E*: metrics used to quantify how biomechanical cost and path length influence subject choices. Circles show the percentage of T1 choices as a function of relative path length (logarithm of length ratio $D_1/D_2$) for T1M (filled) and T1m (open) arrangements. Solid and dashed lines are logistic fits through these points. To characterize the effect of relative path length, we calculate the maximum vertical range (MVR) of the T1M and T1m data, and to characterize the effect of biomechanics, we calculate the area (*A*) between the T1M minus T1m curves.

hand displacement. In brief, movements along the major axis of the ellipse are easy and require little effort, whereas movements along the minor axis require more effort. Note that because the via-points are in opposite directions from the origin, the radius of the ellipse along both directions is the same, implying that the biomechanical cost of the initial part of the movement (until the via-point) is very similar for both movement choices, in both T1M and T1m arrangements. However, the movements differ at the end: in the T1m arrangement, arrival at T1 is along the minor axis, making it more difficult than arrival at T2. The converse is true in the T1M arrangement. In addition to manipulating the biomechanical costs of moving to T1 vs. T2, we also varied the length of movement to each target along the path from the center and through the via-point. The total path lengths to T1 vs. T2 were 9 vs. 13 cm (33% of trials), 11 vs. 11 cm (33%), or 13 vs. 9 cm (33%). In the one-target trials, only a single via-point and target appeared, chosen randomly from the four equal-path length cases (T1 or T2; T1M or T1m; 11 cm). Subjects were instructed to choose the movement that "feels most comfortable," passing through the via-point and through the target. Subjects were not required to stop in the target. The trial was considered an error if the reaction time was longer than 200 ms or if the stylus reached the target before first crossing over the via-point. During the movement, the stylus position was continuously indicated by a small cross, and the via-point and target cues changed to green as the stylus slid over them. Trials were separated by a 500-ms intertrial interval.

In the TMS sessions (Fig. 1*C*), the task was similar, except that the observation interval was always 500 ms, the targets were blue circles 2 cm in diameter, and subjects were instructed to stop in them for a target hold time (THT) of 500 ms. The intertrial interval was 3,000 ms. In each of the two TMS sessions, subjects performed 6 blocks of 132 trials. Each block contained 12 one-target trials, 4 of which were baseline stimulation trials (TMS applied 1 ms after stimulus onset), and 120 two-target trials. Among the 120 two-target trials there were 20 repetitions of each of the 6 target arrangements. TMS was applied on half of these, twice at each of the 5 stimulation times (150, 200, 250, 300, or 350 ms). Thus each subject performed 24 trials (2 sessions × 6 blocks × 2 repetitions) at each arrangement and stimulation time. To quantify the CSE in each condition, we recorded electromyographic (EMG) activity in six arm muscles and calculated the magnitude of MEPs caused by the TMS pulse.

*EMG recording.* EMG activity was recorded from three flexors, pectoralis major (PEC), biceps long head (BIC), and brachioradialis (BRA), and three extensors, triceps lateral head (TRIA), triceps long head (TRI), and posterior deltoid (DEL). EMGs were measured with disposable MT-130 surface electrodes, bandpass filtered (10–400 Hz), amplified (×1,000) by an 8-channel Lynx-8 instrumentation amplifier (Neuralynx, Bozeman, MT), and sampled at 1,000 Hz by an acquisition card (National Instruments) installed in a personal computer running Windows XP (Microsoft, Redmond, WA). Maximum voluntary contraction (MVC) was estimated at the beginning of each session for each subject as the average of the peak-to-peak EMG amplitude during three maximal contractions of each muscle. This measure was used to normalize the EMG activity recorded in each muscle during the reaching movements. Although we recorded from all six muscles, for the analysis of MEPs we focused on the raw DEL and TRI signals (before normalization), because these two muscles proved to be clear agonists for movements toward T1 (see Fig. 3), strongly discriminating between the two movements. We

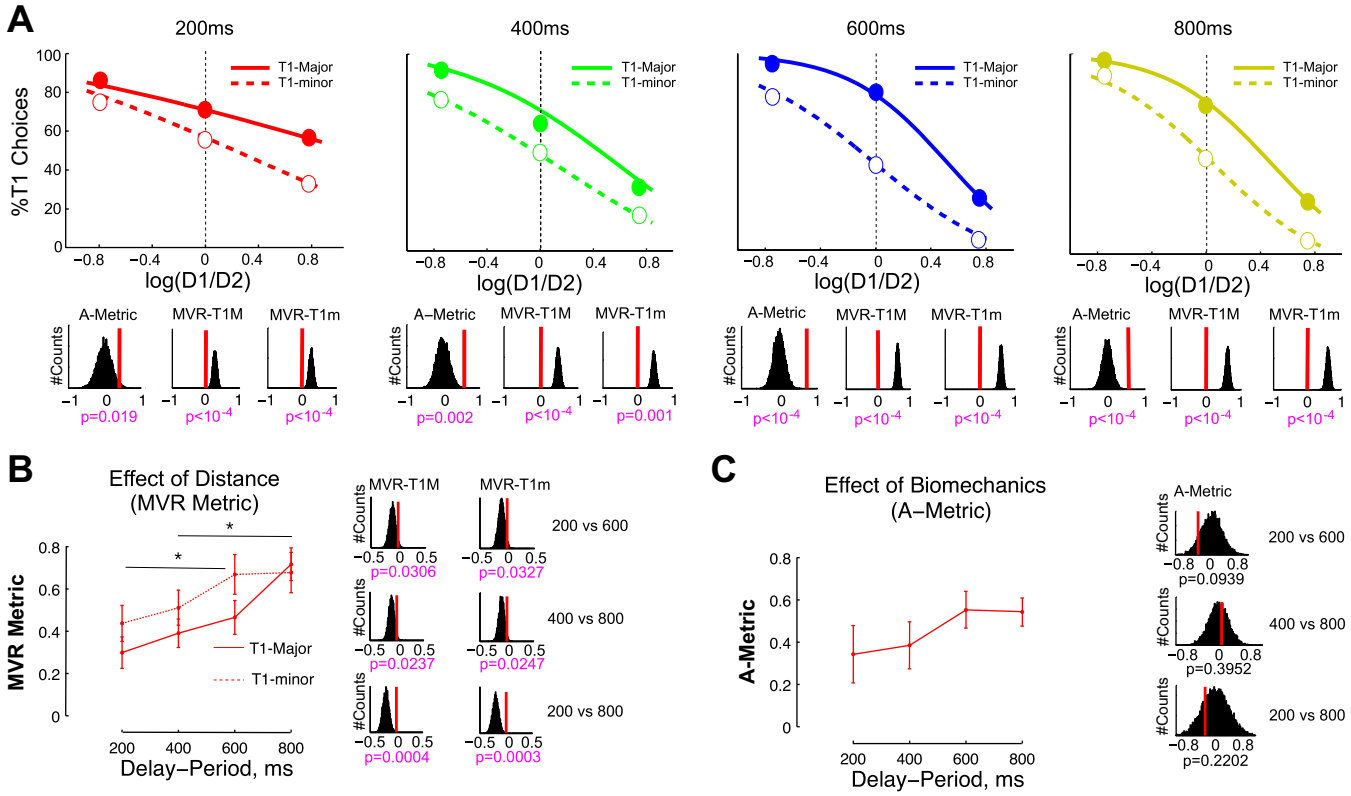


Fig. 2. Results from the behavioral sessions. *A*: the percentage of T1 choices as a function of relative path length for T1M (filled circles and solid line) and T1m arrangements (open circles and dashed line) for each observation interval. Below each plot, the *left* histogram shows the distribution of the shuffled A-metric compared with the real unshuffled value (red vertical line), and the *P* value indicates significance. The *middle* and *right* histograms compare the shuffled values of the MVR-metric to zero, for T1M and T1m data, respectively. *B*: comparison of the MVR-metrics (T1M, solid; T1m, dashed) for different observation intervals (*left*). Histograms (*right*) show bootstrap comparisons of the differences between 3 pairs of intervals for which the difference was significant. Red line indicates zero difference. *C*: comparison of A-metrics for different observation intervals (*left*). Histograms (*right*) show bootstrap comparisons between intervals, none of which are significant.

had no recordings of comparably clear agonist activity for movements toward T2.

*Single-pulse TMS.* Throughout the TMS sessions, subjects used a chin rest to reduce head motion and wore a tightly fitted electroencephalography (EEG) cap. A figure-of-eight coil (7-cm diameter of wings) connected to a Magstim Rapid stimulator (Magstim, Whitland, UK) was placed tangentially on the scalp with the handle oriented toward the back of the head and 45° away from the midline, approximately perpendicular to the central sulcus. We identified the optimal spot for eliciting MEPs in the TRI and the DEL with single TMS pulses (1-ms duration). This location was marked on the EEG cap to provide a reference point throughout the experimental session. The resting motor threshold (rMT) was defined as the minimum TMS intensity necessary to evoke MEPs of ~50 $\mu$V peak to peak in the Tri in 5 of 10 consecutive trials. The mean rMT was 57.45% (SD 4.5) of the maximum stimulator output. The intensity of the TMS for the experimental sessions was always 115% of rMT, set for each subject at the beginning of each individual session.

The amplitude of MEPs was quantified in each trial using the "peak-to-peak" method, which measured the difference between the maximum and minimum values of unrectified EMG within a time interval of 15–35 ms after the TMS pulse. This interval proved to be optimal for MEPs recorded in proximal muscles. The MEPs were transformed into *Z* scores (by subtracting the mean MEP amplitude for each individual session and dividing by the standard deviation of the MEPs) and then normalized to the baseline (MEPs evoked at 1 ms after stimulus presentation). Trials in which voluntary contraction of DEL or TRI overlapped with the evoked potential were discarded from MEP analyses.

*MEP and EMG correlation analysis.* One concern about MEPs is that they could partly reflect EMG activation, rather than an element of cortical activity, before EMG activation. To control for this possibility, we performed a correlation analysis between the MEP peak-to-peak amplitudes and the EMG amplitude of the corresponding muscle, recorded during the same time window. We performed this analysis for the DEL and TRI for each individual subject.

*Analysis of target preference.* Figure 1*E* illustrates how we quantified the effects of path length and biomechanical cost on subject choices. We calculated the proportion of trials for which subjects chose T1 over the total number of choices to obtain a measure of each subject's preference for T1, for each of the possible relative T1/T2 path lengths. The proportion of T1 choices for each biomechanical configuration (T1M and T1m) was plotted on a logarithmic scale and fitted with a sigmoidal curve as described by *Eq. 1*:

$$P_{T1}(Q) = \frac{e^{Q}}{1 + e^{Q}} \qquad Q = a \times \log\left(\frac{D_1}{D_2}\right) + b \qquad (1)$$

where $a$ and $b$ are free parameters and $D_1$ and $D_2$ are the path lengths measured from the starting point through the via-point and to the target. If path length has an effect, we expect these sigmoids to have a negative slope, and characterize the magnitude of the effect using the maximum vertical range (MVR) of the data for T1M and T1m separately. If biomechanical cost has an effect, we expect the curve for T1M to be shifted to the right of the curve for T1m. We characterize its magnitude by calculating the area (*A*) below the curve for T1M and above the curve for T1m. Bootstrapping was used to assess statistical significance of these metrics. In brief, we generated a distribution of 10,000 A-metrics computed from randomized data sets in which the preference values were randomly shuffled. If the unshuffled value of the A-metric was greater than 95% of the distribution of shuffled A-metrics, the result was considered significant at $P < 0.05$. To assess whether the MVR was significantly larger than zero, we calculated the distribution of randomly shuffled data for each individual sigmoid and checked whether 95% of that distribution of shuffled MVR metrics was higher than zero. If that was the case, the result was considered significant at $P < 0.05$. We used similar bootstrapping techniques to assess the growth of the A-metric and MVR-metric across different observation intervals (Efron 1982).

Our calculation of net muscle work is described in detail in Cos et al. (2011). In brief, using a simplified two-segment rigid body model of the arm, we calculated the integral of the muscle work (subtracting out the contribution of interaction torques) along the path from the starting point to the target through the via-point for each joint. We then added the muscle work calculated for each joint to obtain the estimate of total muscle work. These estimates for each movement are indicated in milliJoules (mJ) near each target in Fig. 1*D*.

*Analysis of the influence of biomechanics and path length on CSE.* To assess the effects of path length and biomechanical costs on CSE, we analyzed the *z*-normalized MEP amplitudes at each stimulation time by means of a four-way analysis of variance (ANOVA) with the following factors: biomechanics (B: T1M or T1m), path length (or distance) to target T1 (D: 9, 11, or 13 cm), chosen target (C: T1 or T2), and muscle (M: DEL or TRI). The criterion of significance was $P < 0.05$. For main effects and interactions that met significance according to the ANOVA, we also performed paired *t*-tests corrected for multiple comparisons (Bonferroni) on the MEP distributions.

## RESULTS

*Movement preference as a function of observation interval.* As in our previous studies, subjects exhibited a preference for moving to targets closer to the starting point and along paths requiring lower biomechanical effort. To quantify these effects, we pooled together the data from all eight subjects of our first experiment as a function of the observation interval (200, 400, 600, or 800 ms) and calculated the preference curves for T1 for each of the two arrangements (T1M and T1m) as a function of the relative path length to the targets (see Fig. 1, *D* and *E*). Similar to our previous results with a 1,000-ms observation interval (Cos et al. 2011, 2012), the preference for T1 exhibited a significant shift between the T1M and T1m arrangements (bootstrap test, $P < 0.05$; see METHODS), indicating that subjects are biased to select movements with lower biomechanical effort. Remarkably, this was significant for all observation intervals (for 7/8 subjects; see Fig. 2*A*). Hence, biomechanical

Table 1. *Main effects and interactions of factors*

| Factor | 150 ms | 200 ms | 250 ms | 300 ms | 350 ms |
|---|---|---|---|---|---|
| B | 0.5527 | **0.0211** | **0.00211** | 0.0969 | 0.7450 |
| D | 0.1072 | **0.0290** | 0.2973 | **0.0007** | 0.0638 |
| C | **0.0002** | **0.0000** | **0.0000** | **0.0000** | **0.0000** |
| M | 0.7839 | 0.6390 | 0.8388 | 0.9721 | **0.0147** |
| B+D | 0.1241 | 0.3093 | **0.0292** | 0.0805 | 0.1488 |
| B+C | **0.0010** | **0.0016** | 0.0825 | 0.1232 | 0.8931 |
| B+M | 0.4406 | 0.7378 | 0.8583 | 0.2262 | 0.2772 |
| D+C | **0.0116** | **0.0007** | 0.1406 | **0.0011** | **0.0363** |
| D+M | 0.8133 | 0.4111 | 0.9328 | 0.7351 | 0.9539 |
| C+M | 0.1792 | 0.1101 | 0.3510 | 0.5018 | 0.6935 |
| B+D+C | 0.4610 | 0.2927 | 0.3977 | 0.1733 | **0.0069** |
| B+D+M | 0.8432 | 0.5033 | 0.8357 | 0.7474 | 0.6388 |
| B+C+M | 0.3165 | 0.1669 | 0.6914 | 0.2788 | 0.2731 |
| D+C+M | 0.1910 | 0.5002 | 0.9309 | 0.8872 | 0.8957 |
| B+D+C+M | 0.6270 | 0.6287 | 0.7201 | 0.8423 | 0.7421 |

*P* values for main effects and interactions at 5 transcranial magnetic stimulation (TMS) times were obtained from 4-way analysis of variance performed on motor-evoked potential (MEP) amplitudes with the following factors: biomechanics [B: T1-Major (T1M) or T1-minor (T1m)]; path length to target T1 (D: 9, 11, or 13 cm); chosen target (C: T1 or T2), and muscle (M: posterior deltoid or triceps long head). Bold values indicate statistical significance ($P < 0.05$).

factors were very quickly predicted from the stimulus display and influenced the choice even if the targets and via-points were visible for only 200 ms before movement onset.

However, as can be seen in Fig. 2*A*, the influence of biomechanics and path length (measured using differences between preference curves for T1M and T1m arrangements) did not remain stable across the different observation intervals. In particular, the bias for shorter relative path length (quantified by the MVR metric; see METHODS) was significantly stronger at 600 and 800 ms than it was at 200 ms (Fig. 2*B*; bootstrap test, $P < 0.05$) for both T1M and T1m arrangements. In contrast, the biasing effect of biomechanics (quantified by the A-metric; see METHODS) remained relatively similar as the duration of the observation interval expanded (Fig. 2*C*). In summary, the subjects' preference for shorter and biomechanically easier movements took as little as 200 ms to develop, and the preference for shorter movements became gradually stronger as time passed.

It is worth mentioning that, in addition to the biomechanical and path distance factors, all subjects exhibited a mild directional bias. Hence, the sigmoids on Fig. 2*A* are not necessarily centered on zero. Nevertheless, since our emphasis is analyzing the influence of the biomechanical factors, we primarily focused on the shift between the T1M and T1m sigmoids.

*Time course of the influence of biomechanics and path length on CSE.* To test how the CSE was influenced by biomechanical ease and relative path length, as well as target choice and muscle, we first performed a four-way ANOVA on the *z*-normalized MEP amplitudes obtained at each stimulation time (150, 200, 250, 300, and 350 ms) with the following factors: biomechanics (B), path length to T1 (D), chosen target (C), and muscle (M). The results are summarized in Table 1 as *P* values for each main effect or interaction at each of the five TMS stimulation times. First, note that the factor muscle had a significant main effect only at 350 ms, and there was no significant higher-order interaction with the other factors. Hence, in subsequent analyses we collapsed data across the two muscles across all subjects. Second, note that the chosen target exerted a very significant effect on *z*-normalized MEPs at all stimulation times, because both muscles were agonists for T1 but not T2 movements (Fig. 3*A*; see also Fig. 3*B* for an illustration of the DEL and TRI *z*-normalized MEPs represented separately or pooled together). Third, the chosen target had a strong interaction with both biomechanics (B+C) and path length (D+C) at the two earliest stimulation times (150 and 200 ms) and with path length at the two latest times (300 and 350 ms). Finally, there was also a significant interaction between biomechanics and path length (B+D) at 250 ms and

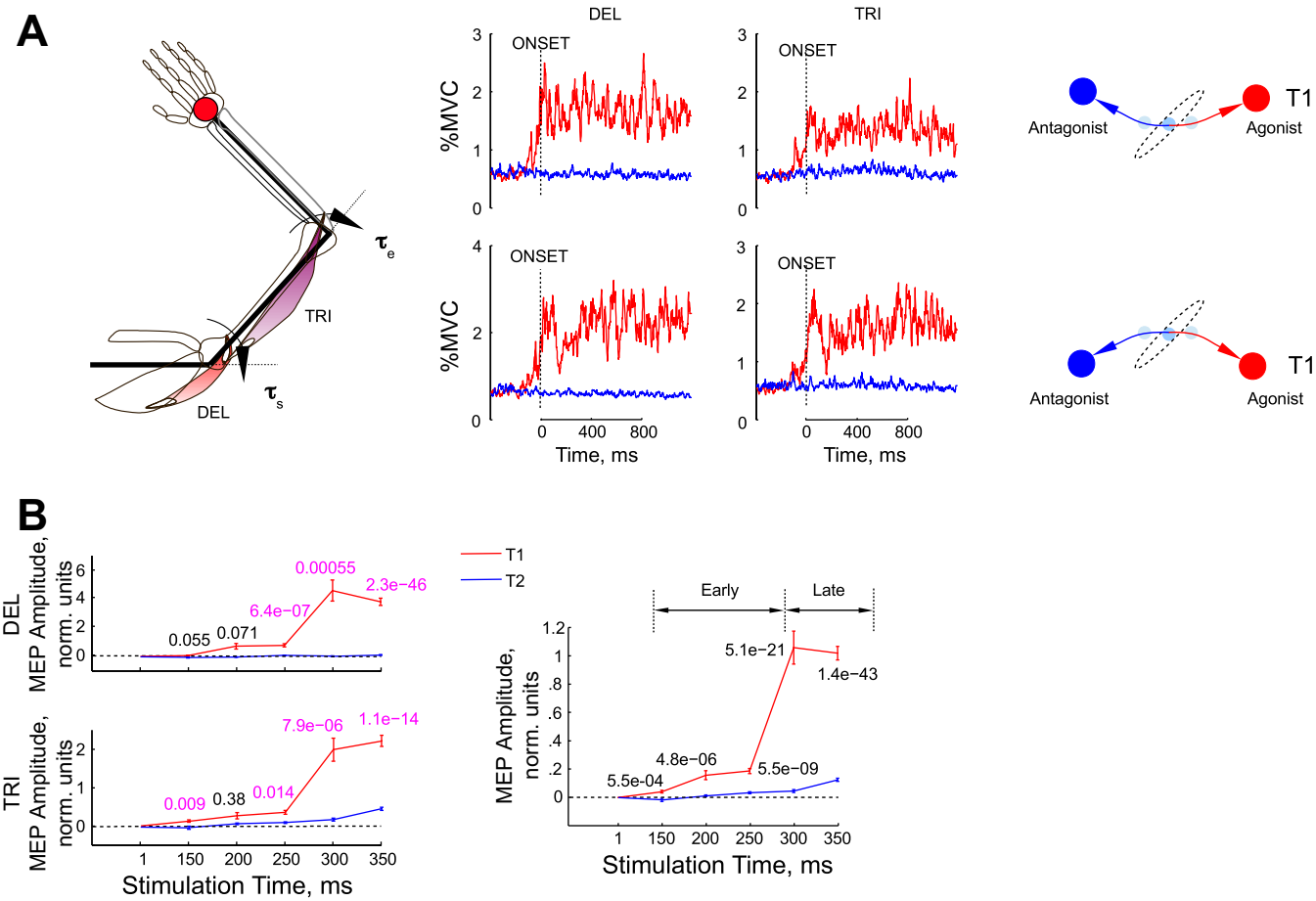


Fig. 3. *A*: electromyographic (EMG) activity of the posterior deltoid (DEL) and triceps long head (TRI) for T1 (red) and T2 choices (blue) in the T1M (*top*) and T1m arrangements (*bottom*), expressed as a percentage of the maximum voluntary contraction (MVC) of each muscle. Vertical dashed line indicates movement onset. *B*, *left*: normalized motor-evoked potential (MEP) amplitude of DEL (top) and TRI (bottom) as a function of stimulation time, showing the mean and SE across all T1 choice (red) and T2 choice (blue) trials. Numbers indicate *P* value of Kolmogorov-Smirnov (KS) test applied to the distribution of MEPs in T1 vs. T2 choice trials. *Right*, pooled data from both muscles. norm., Normalized.

a significant three-way interaction between biomechanics, path length, and choice (B+D+C) at 350 ms. In the following paragraphs, we examine each of these effects and interactions in detail.

Figure 4, *A* and *B*, shows the interaction effect of biomechanical cost and choice on MEPs in a single subject (in mV) or across subjects (in mV and after normalization) for T1 (*A*) and T2 choices (*B*) in the T1M (red) and T1m (blue) arrangements (data are pooled across both muscles). When T1 was chosen (Fig. 4*A*), MEPs measured at 150 ms were larger when T1 was the biomechanically easier target (T1M; red) than when it was the harder target (T1m; blue). This relationship reversed at 200 and 250 ms, with larger MEPs when T1 required more effort than T2 (T1m, red). The effect was reversed when T2 was chosen (Fig. 4*B*), because MEPs measured at 150 ms were smaller when T2 was the biomechanically harder target (T1M; red) than when it was the easier target (T1m; blue).

A similar reversal between 150 and 200 ms was observed when the interaction effect of distance and choice on MEPs was examined (Fig. 5, *A* and *B*). When T1 was chosen, MEPs at 150 ms were larger when T1 was closer than when T2 was closer (Fig. 5*A*). In contrast, MEPs at 200 ms were larger when T1 was further than T2. In other words, the MEPs exhibited a reversal between 150 and 200 ms as a function of relative path length. In a complementary fashion, when T2 was chosen, the MEPs at 150 ms exhibited a tendency to be larger when T2 was closer than T1 (Fig. 5*B*). In contrast, MEPs at 200 ms were larger when T2 was further than T1.

Additional interaction effects were reported by the ANOVA for later MEPs, such as B+D at 250 ms and B+D+C at 350 m. The interaction between biomechanics and distance irrespective of target chosen (B+D) exhibited a reversal at 250 ms (data not shown). The MEPs were stronger when T1 was closer than T2 in the T1M arrangement, and the reverse was seen in the T1m arrangement. The three-way interaction (B+D+C) at 350 ms is shown in Fig. 6. When T1 was selected despite being far, MEPs were larger in the T1M arrangement (red) than in the T1m arrangement (blue). However, these relationships reversed when T1 was close, with larger MEPs in the T1m arrangement. When T2 was chosen, all of these effects were inverted (Fig. 6, *bottom*).

*The transition from competition to implementation.* To summarize the results so far, we observed two main trends in the MEPs as a function of stimulation time. At 150 ms after targets and via-points appeared, MEPs were generally larger for those movements that subjects tended to prefer (when T1 was in the major arrangement and/or was the closer target). However, later in the trial, this effect disappeared, and the MEPs appeared to become more closely related to the muscular effort associated with the chosen movement (i.e., larger MEPs when T1 requires more effort). This was clearly seen for the influence of biomechanics (Fig. 4*A*), reaching significance at 200 and 250 ms (a trend seen for all 8 subjects). However, it was not consistent for the effect of path length (Fig. 5*A*): at 200 ms, the MEPs were higher for the far than the close targets (6/8 subjects), as predicted, but this did not persist and even

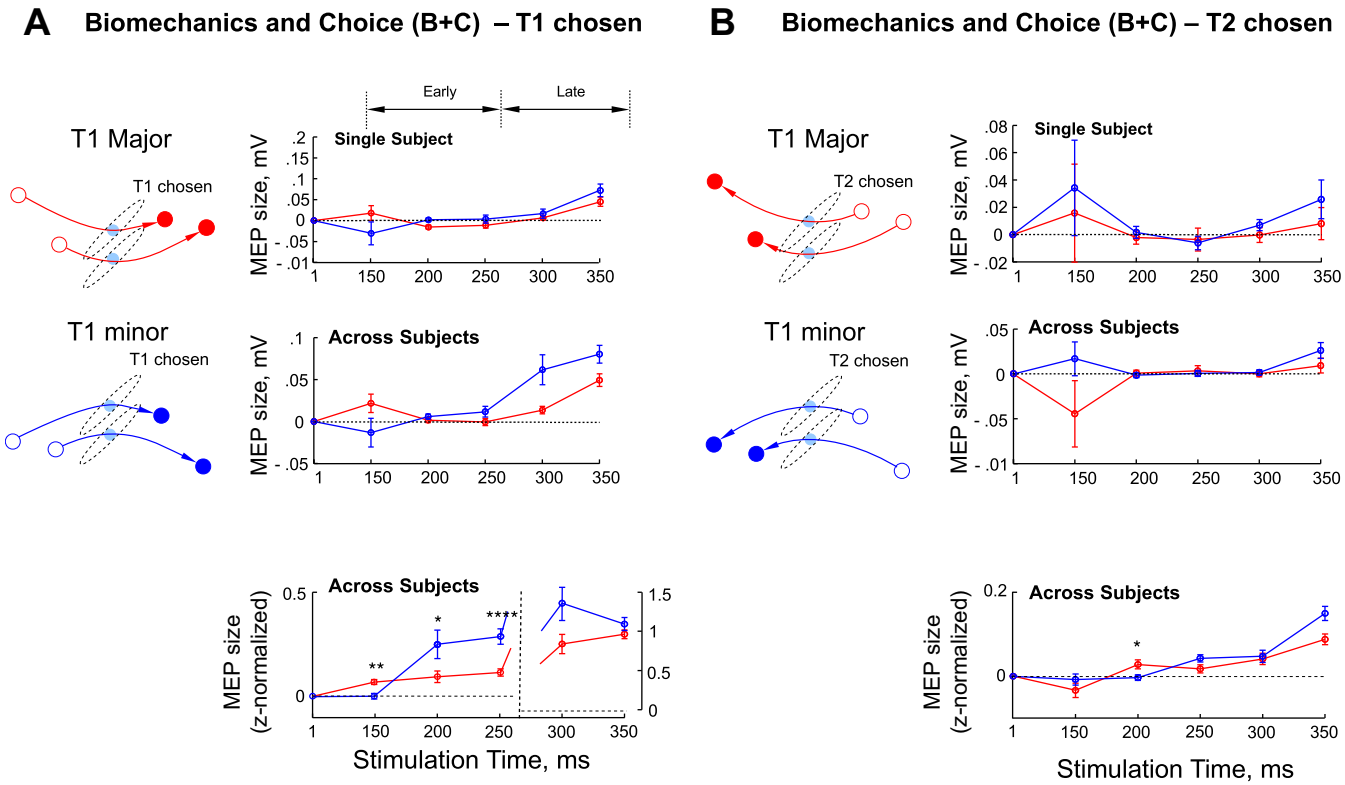


Fig. 4. *A*: MEP amplitudes expressed in mV for a typical subject (*top*), averaged across subjects (*middle*), and *z*-normalized with respect to baseline (*bottom*) as a function of biomechanics (B) and chosen target (C) for trials in which T1 was selected. Red lines show data from the T1M arrangement pooled across different distances. Blue lines show data from the T1m arrangement pooled across distances. To better assess the effect of biomechanics during the early delay period, we magnified the *y*-range for the first 3 (nonbaseline) stimulation times (until the vertical dashed line). *B*: same as *A* for trials in which T2 was selected. In both panels, significant effects (KS test) are indicated (*$P < 0.5$; **$P < 0.01$; ***$P < 0.001$; ****$P < 0.0001$).

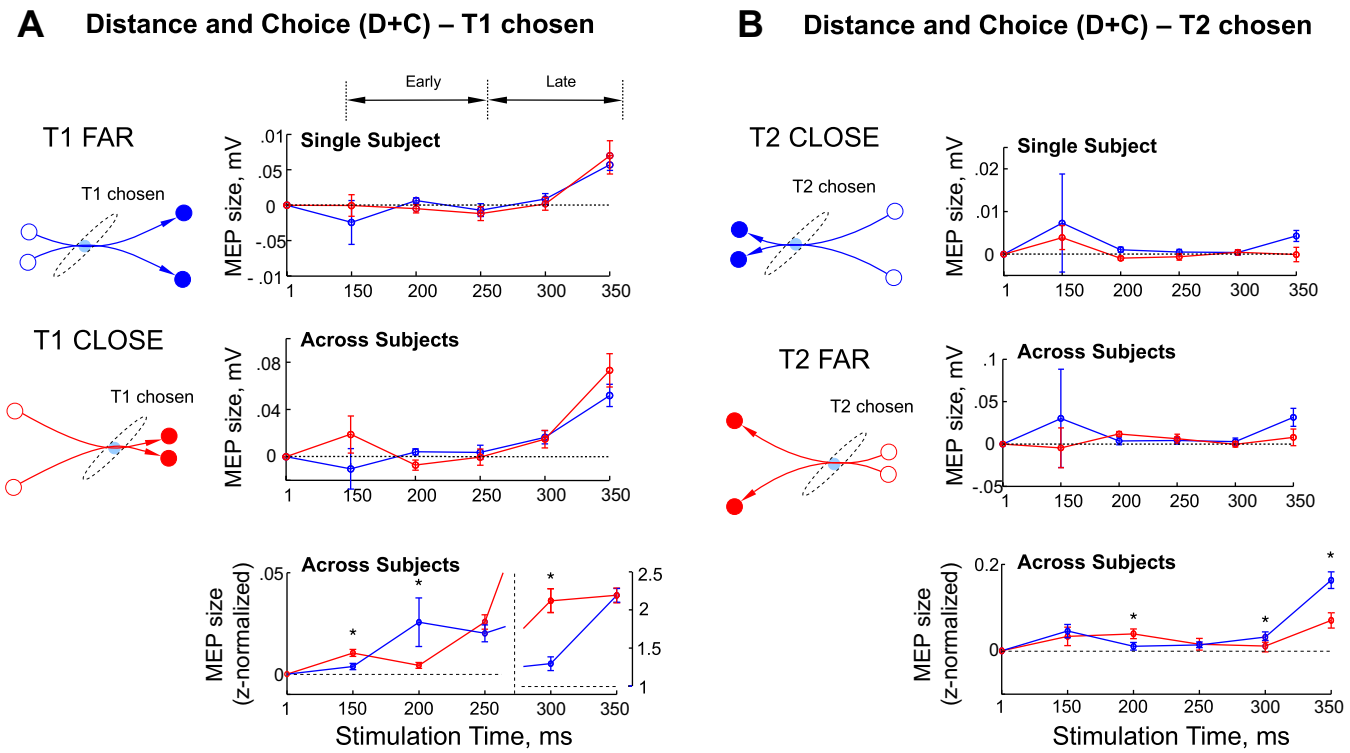


Fig. 5. *A*: MEP amplitudes expressed in mV for a typical subject (*top*), averaged across subjects (*middle*), and *z*-normalized with respect to baseline (*bottom*) as a function of path length to T1 (D) and chosen target (C) for trials in which T1 was selected. Red lines show data from trials when the T1 target was closer than T2 pooled across T1M and T1m arrangements. Blue lines show data when T1 was further than T2. To better assess the effect of distance during the early delay period, we magnified the *y*-range for the first 3 stimulation times (until the vertical dashed line). *B*: same as *A* for trials in which T2 was selected. In both panels, significant effects (KS test) are indicated (*$P < 0.5$; **$P < 0.01$; ***$P < 0.001$; ****$P < 0.0001$).

reversed (for 4/8 subjects as well as for the normalized average) at 300 ms. We do not presently have an explanation for this finding, which should be further explored in future research.

Finally, we investigated how well the *z*-normalized MEPs at each stimulation time correlated with the subject's preference and/or with the muscular effort associated with the impending movement. First, we calculated the relative MEP amplitude as the difference between the *z*-normalized MEPs during T1 vs. T2 choices in each of the six arrangements of targets. We also estimated the relative energetic demand for the two potential movements as the difference in net muscle work to each target in each arrangement (see Fig. 7*A*). Based on these, we performed two regression analyses. The first examined how relative MEP amplitude predicts subject choices (Fig. 7*B*). The second examined how it varies as a function of the relative energetic demand required by movements to T1 vs. T2 (Fig. 7*C*). Consistent with the results described above, at 150 ms there was a significant positive relationship between the relative MEP amplitude and the probability of choosing T1 ($R^2 = 0.87$, $P = 0.0017$) and a significant negative relationship between the relative MEP amplitude and the relative energetic demand ($R^2 = 0.87$, $P = 0.0011$). In other words, the relative MEP amplitude at 150 ms covaried with the subjects' preference for movements that required less energy. At 200 ms, both of these relationships reversed (probability of choosing T1: $R^2 = 0.73$, $P = 0.045$; relative energy: $R^2 = 0.73$, $P = 0.031$), and relative MEP amplitude more closely reflects the energetic cost of the movement that will be chosen. The correlations seen at 200 ms did not remain significant later in the trial, possibly because the gains of our muscles were significantly different when acting as agonists to T1 than when acting as antagonists to T2.

*Controlling for the impact of EMG activation on MEP amplitudes.* We recorded MEPs from two proximal muscles during a delay period. To minimize the possibility of contamination of MEPs by the underlying EMG activation, we eliminated those trials in which EMG activation was within 50 ms of the MEP. Furthermore, to provide a quantitative control of the effectiveness of this method, we performed a correlation analysis between MEP amplitudes and EMG activations, recorded during the same time window. The resulting *P* values for each muscle and stimulation time are shown in Tables 2 and 3. In summary, for the two times of interest, 150 and 200 ms, only 1/16 (6.75%) cases exhibited some significant correlation at 150 ms and only 2/16 (13.5%) at 200 ms ($P < 0.05$). Hence, for the interval of interest in this study, MEPs and EMGs can be safely considered uncorrelated.

## DISCUSSION

While studies of decision-making have traditionally focused on the kinds of cognitive decisions that characterize human economic choices, the neural mechanisms underlying decision-making evolved long before abstract cognitive abilities. At the time the relevant neural circuits were being established, most decisions were between concrete actions such as run left vs. right or reach for one branch or another. Making such "embodied decisions" entails more than just abstract representations of outcome value and includes a wide variety of senso-

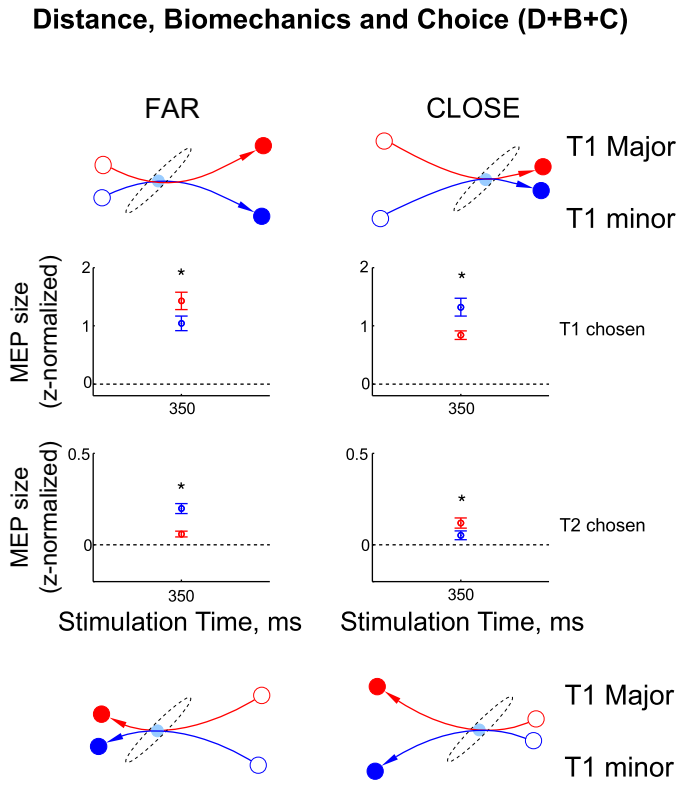


Fig. 6. Normalized MEP amplitudes ($z$-normalized) as a function of path length to T1 (D), biomechanics (B), and chosen target (C), evaluated at 350 ms. Red lines show data from T1M and blue from T1m. Significant effects (KS test) are indicated (*$P < 0.5$; **$P < 0.01$; ***$P < 0.001$; ****$P < 0.0001$).

rimotor contingencies, such as the ease of a movement or its energy requirements. This may explain why many neurophysiological studies have consistently found correlates of decision variables within the same sensorimotor circuits that are involved in the planning and online guidance of movement (Cisek and Kalaska 2010; Gold and Shadlen 2007; Hernández et al. 2010). For example, while a decision is being made, neural activity in parietal and premotor regions of the oculomotor and arm movement systems encodes the potential actions in parallel (Baumann et al. 2009; Cisek and Kalaska 2005; Klaes et al. 2011; McPeek and Keller 2002) and is modulated by many factors relevant for a choice, including expected gain (Glimcher 2002; Pastor-Bernier and Cisek 2011), local income (Sugrue et al. 2005), and probability (Thura and Cisek 2014; Yang and Shadlen 2007). Furthermore, the interactions between potential targets depend on their spatial similarity (Pastor-Bernier and Cisek 2011), consistent with a competition that takes place in a sensorimotor map representing possible movement parameters. These results can be explained by models (e.g., Cisek 2007) in which potential actions compete against each other in the sensorimotor system, and this competition is biased by influences arriving from other regions, including outcome value estimates from orbitofrontal cortex (Padoa-Schioppa 2011), action value computation from anterior cingulate cortex (Kennerley et al. 2011), selection rules from dorsolateral prefrontal cortex (Miller 2000; Miller et al. 2002; Tanji and Hoshi 2001), and biasing signals from the basal ganglia (Redgrave et al. 1999).

In the present study, we investigated how a competition between two potential reaching actions is biased by information about their kinematic and kinetic costs. We expected that information about the relative path length would be processed very quickly because it presumably involves the fast dorsal visuomotor stream. In contrast, we expected that computing the more subtle biomechanical costs of the potential movements would take more time, assuming that it involves sophisticated computation through mental rehearsal or a predictive "forward model" (Jordan and Rumelhart 1992; Miall and Wolpert 1996).

Contrary to our expectations, the biasing effect of biomechanics was in fact very fast. As shown in Fig. 2*A*, the effect of biomechanics was significant even if subjects were only given 200 ms to view the stimulus display before initiating movement. In further contrast to our expectations, although the effect of biomechanics was equally strong at all observation intervals, the effect of relative path length became stronger between 200 and 600 ms. One explanation for this phenomenon is that the influence of path length on choices was not related to a purely spatial preference, as we initially hypothesized, but that it too was due to a preference for movements requiring less energy. However, because path length has only a small effect on the total energetic demand of a movement, smaller than the effect of biomechanics (Cos et al. 2012), it may thus exert only a weak bias whose influence on the decision develops more slowly and always follows the initial specification of which muscles will produce the movement. It is also relevant that although cells in the dorsal premotor cortex exhibit directional tuning shortly after target appearance, their modulation by path length develops gradually over 200–300 ms (Messier and Kalaska 2000).

In previous studies we conducted an analysis of the contribution of biomechanics and path length to the overall energy associated with each movement (Cos et al. 2011, 2012; see also the work of Dounskaia et al. 2011) and reached a similar conclusion: the direction of movement has a major impact on energetic demand, whereas the impact of path length is relatively small. Indeed, a major factor influencing preferences may be related to the number of joints involved in the movement, since the major axis of the mobility ellipse is mostly coincident with the direction of single-joint movements. Furthermore, in an earlier study (Cos et al. 2012) we examined how the preference for lower biomechanical cost interacted with control constraints, such as target size and the requirement to stop in the target, and found that the addition of both of these constraints reduced the bias associated with biomechanics.

The behavioral results were largely corroborated by the TMS data, which confirmed that the biasing effects of biomechanics and path length were reflected in CSE as early as 150 ms after stimulus presentation. This suggests that TMS can be used to probe the state of an evolving decision between actions involving proximal muscles (deltoid and triceps) as well as the distal muscles (e.g., first dorsal interosseus) used in most studies (Klein et al. 2014; Klein-Flügge and Bestmann 2012; Michelet et al. 2010; van Elswijk et al. 2007).

The speed with which biomechanical and geometric factors appeared to influence subject choices raises the question of what mechanisms may be responsible. Previous studies have shown that neural activity in frontal eye field discriminates pro- vs. anti-saccade instructions in 120 ms (Sato et al. 2003), whereas activity in dorsal premotor reflects an instructed choice within 130 ms of a cue (Cisek and Kalaska 2005). In general, activity patterns across diverse regions of monkey

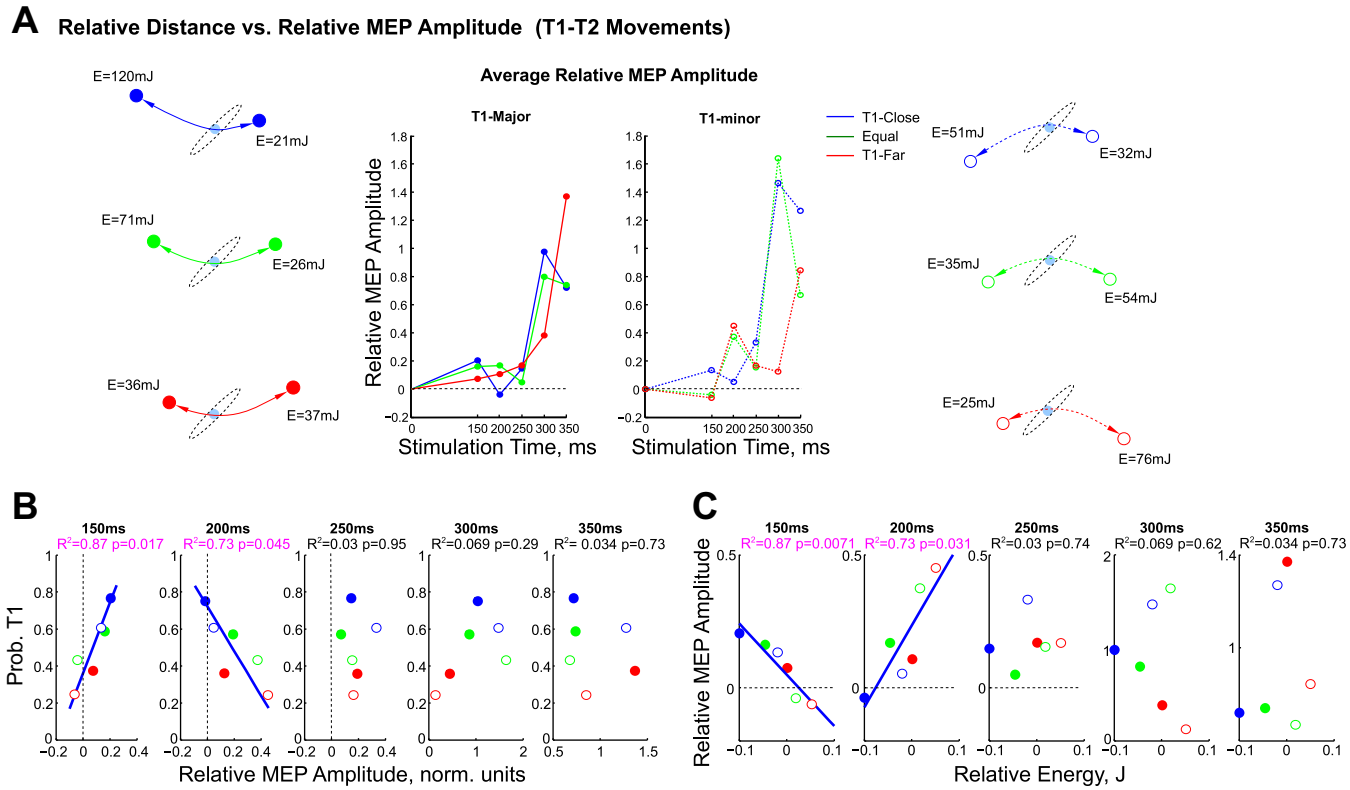


Fig. 7. *A*: the relative MEP amplitude in each of the 6 arrangements plotted as a function of stimulation time. Solid lines indicate T1M arrangement and dotted lines T1m arrangement. Numbers indicate the energy (E, in mJ) required for each movement. *B*: the probability of choosing target T1 in each of the 6 arrangements (Fig. 5*A*) plotted against the relative MEP amplitude in T1 minus T2 trials at different stimulation times. Filled circles, T1M; open circles, T1m; Prob., probability of choosing. Solid lines indicate statistically significant regressions ($P < 0.05$). *C*: the relative MEP amplitude plotted against the relative energy of T1 vs. T2 in each of the 6 arrangements. Again, solid lines indicate statistically significant regressions.

cerebral cortex reflect a simple decision about 150 ms after cue onset (Ledberg et al. 2007). In the present study we found a significant biasing effect on human CSE at around the same time, despite the fact that the biasing factors in our task would seem to require significantly more computation.

We consider two possible explanations for the speed of these effects. First, subjects could have memorized the costs of movements to specific spatial locations and simply recall them when they are presented with target stimuli in those locations. Previous studies have shown that when the physical effort of candidate movements is explicitly indicated by stimulus cues, it quickly modulates neural activity in anterior cingulate cortex (Kennerley et al. 2011) and, to a lesser degree, in basal ganglia (Pasquereau and Turner 2013). Thus it is possible that in the present study subjects simply associated a learned cost with each spatial location. Although we cannot completely exclude this possibility in the present data, comparable behavioral results were found in our earlier studies (Cos et al. 2011, 2012) in which we included a number of controls that made a memory-based strategy unlikely (locations and orientations of targets and starting points were varied randomly, and similar points in space were approached from different directions with different biomechanical costs).

An alternative explanation for the rapidity of the biasing effect is that the brain really is able to compute biomechanical costs very quickly, and the result of this computation can quickly bias activity in the motor cortex. Indeed, if the mechanism that computes the biomechanical costs involves the same forward model that is also used in the online guidance of movement (Jordan and Rumelhart 1992; Miall and Wolpert

Table 2. *Deltoid EMG vs. MEP correlation analysis*

| Subject | 150 ms | 200 ms | 250 ms | 300 ms | 350 ms |
|---|---|---|---|---|---|
| *1* (CB) | 0.42 | 0.36 | 0.36 | 0.39 | 0.47 |
| *2* (LW) | 0.36 | 0.32 | 0.34 | 0.37 | 0.37 |
| *3* (NT) | 0.75 | 0.51 | 0.97 | 0.54 | **0.0011** |
| *4* (RA) | 0.83 | 0.71 | 0.68 | 0.33 | 0.12 |
| *5* (CK) | 0.52 | **0.00094** | 0.61 | 0.54 | 0.56 |
| *6* (BB) | 0.44 | 0.57 | 0.86 | 0.31 | **0.022** |
| *7* (AC) | 0.51 | 0.52 | 0.27 | 0.45 | 0.73 |
| *8* (ND) | 0.32 | 0.96 | 0.87 | **0.012** | 0.73 |

*P* values were obtained from the correlation analysis between MEP amplitudes and electromyographic (EMG) amplitudes at each stimulation time for the deltoid muscle. Bold values indicate statistical significance ($P < 0.01$).

Table 3. *Triceps EMG vs. MEP correlation analysis*

| Subject | 150 ms | 200 ms | 250 ms | 300 ms | 350 ms |
|---|---|---|---|---|---|
| *1* (CB) | **0.0011** | 0.24 | 0.7 | 0.45 | 0.49 |
| *2* (LW) | 0.43 | 0.35 | 0.16 | 0.33 | 0.42 |
| *3* (NT) | 0.13 | 0.55 | 0.93 | 0.24 | **0.00057** |
| *4* (RA) | 0.24 | 0.35 | 0.16 | 0.37 | 0.92 |
| *5* (CK) | 0.32 | **0.0079** | **0.0014** | **0.00072** | **6E-5** |
| *6* (BB) | 0.31 | 0.2 | 0.94 | 0.12 | 0.22 |
| *7* (AC) | 0.22 | 0.92 | 0.99 | 0.039 | 0.48 |
| *8* (ND) | 0.21 | 0.051 | 0.31 | **0.014** | **0.033** |

*P* values were obtained from the correlation analysis between MEP amplitudes and EMG amplitudes at each stimulation time for the triceps muscle. Bold values indicate statistical significance ($P < 0.01$).

1996), then it would clearly have to be very fast. Nevertheless, it is interesting to note that in a pilot study with a version of our task in which subjects were free to respond at any time, we did not observe a significant influence of biomechanics (unpublished observations). It is possible that subjects preferred to save time by making early decisions, too early for the subtle effects of biomechanics to bias their choices.

Although CSE at 150 ms was well correlated with the choice of the selected movement, that relationship apparently reversed at 200 ms (Fig. 7). There is a straightforward potential explanation for this phenomenon. Previous work has shown that MEPs scale nearly linearly with impending EMG activity well before EMG onset (MacKinnon and Rothwell 2000). Therefore, since EMG is larger for movements requiring larger energy, it follows that MEPs evoked before movement onset will scale with the energy of the imminent movement. Thus what we see in the time course of CSE (Figs. 4–6) may reflect the shifting influence of two factors: First, early in the trial, we see the biasing influence of factors that determine the subject's choice, which is made very rapidly after stimulus onset. Once the decision is made, subjects can begin to prepare the muscle commands that will initiate the movement, in anticipation of the highly predictable GO signal. At this time, CSE becomes dominated by preparatory activity, which is higher during trials in which the agonist will demand more energy.

## ACKNOWLEDGMENTS

We thank Gary Duncan for the use of the TMS equipment and Emmanuel Guigon and Benoît Girard for comments on an earlier version of the manuscript.

## GRANTS

This work was supported by an National Sciences and Engineering Research Council Discovery Grant and Canadian Institutes of Health Research, Collaborative Research in Computational Neuroscience Grant 103332 (P. Cisek), the Fonds National de la Recherche Scientifique (J. Duque), and a Ville de Paris HABOT-Project grant (I. Cos).

## DISCLOSURES

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

## AUTHOR CONTRIBUTIONS

I.C., J.D., and P.C. conception and design of research; I.C. performed experiments; I.C. analyzed data; I.C., J.D., and P.C. interpreted results of experiments; I.C. prepared figures; I.C., J.D., and P.C. drafted manuscript; I.C., J.D., and P.C. edited and revised manuscript; I.C., J.D., and P.C. approved final version of manuscript.

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