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ORIGINAL ARTICLE

Identification of a Brain Network Underlying the Execution of Freely Chosen Movements

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Abstract

Action selection refers to the decision regarding which action to perform in order to reach a desired goal, that is, the “what” component of intention. Whether the action is freely chosen or externally instructed involves different brain networks during the selection phase, but it is assumed that the way an action is selected should not influence the subsequent execution phase of the same movement. Here, we aim to test this hypothesis by investigating whether the modality of movement selection influences the brain networks involved during the execution phase of the movement. Twenty healthy volunteers performed a delayed response task in an event-related functional magnetic resonance imaging design to compare freely chosen and instructed unimanual or bimanual movements during the execution phase. Using activation analyses, we found that the pre-supplementary motor area (preSMA) and the parietal and cerebellar areas were more activated during the execution phase of freely chosen as compared to instructed movements. Connectivity analysis showed an increase of information flow between the right posterior parietal cortex and the cerebellum for freely chosen compared to instructed movements. We suggest that the parieto-cerebellar network is particularly engaged during freely chosen movement to monitor the congruence between the intentional content of our actions and their outcome.

Key words: cerebellum, delayed response task, forward model, free choice, posterior parietal cortex, preSMA

Introduction

Action selection, which consists in deciding which movement to perform to reach a desired goal, is essential to achieve a wide range of behaviors. These goal-directed actions can be classified according to a continuum, from externally triggered to internally generated movements (Passingham 2007; Haggard 2008, 2019). In externally triggered movements, the agent's response is determined by an environmental stimulus. By contrast, internally generated (or freely chosen) actions are the expression of the agent's intentionality as they are not constrained by external factors, at least not entirely (Haggard 2019). We have the intu-

ition from our everyday life experience that action selection, whether it is freely chosen or instructed, occurs before movement execution, during a deliberation phase that precedes the action. Accordingly, action selection is thought to participate in the preparation of intentional actions along with several other steps, each of them being either internally generated or externally triggered (Brass and Haggard 2008; Haggard 2008): What action should I perform (“what” component of action selection)? When should I do it (“when” component)? Should I really perform it in the end (“whether” component)? The “what” component is of particular interest, as it is the first crucial aspect

of voluntary actions in the usual sequence of choices. Patients with involuntary movements can no longer match the “what” component of intention to the action’s results, making their movement feel involuntary. Studying brain networks involved in controlling the “what” component of intentional movement is primordial to deepen our understanding of the way our brain links intentional content of our action to their effects in the outside world.

The brain networks underlying the preparation of freely chosen movements as compared to instructed movements have received much attention: Although the situations explored in the laboratory are reductive and simplistic, they contribute to improve our knowledge about human volition (Haggard 2008, 2019; Hallett 2016). Several neuroimaging and electrophysiological studies in humans and nonhuman primates have investigated the preparation of freely chosen movements (Okano and Tanji 1987; Romo and Schultz 1987; Kurata and Wise 1988; Deiber et al. 1996; Cunnington et al. 2002; Waszak et al. 2005; Cui and Andersen 2007; Pesaran et al. 2008; Ariani et al. 2015; Zapparoli et al. 2017, 2018). Regarding the specific step of action selection (or “what” component), freely choosing between different movement possibilities as opposed to being instructed to perform one particular movement recruits a large fronto-mesial network including the supplementary motor area (SMA) and the anterior cingulate cortex (ACC), as well as the middle and inferior frontal gyrus, the ventral premotor cortex, the posterior parietal cortex (PPC, including the inferior parietal lobule and the supramarginal gyrus), the insula, the cerebellum, and the middle temporal gyrus (Ariani et al. 2015; Zapparoli et al. 2017, 2018).

However, it is not known whether the way a movement is selected (freely chosen or instructed) during the preparation phase could influence the subsequent execution phase and the underlying brain network. Since the discovery of the homunculus (Rasmussen and Penfield 1947), the areas involved in motor execution are considered a rather simple push-button system. Most of the previous studies on the subject implicitly postulated that movement execution and the underlying brain activity should be unaffected by whether the movement was freely chosen or instructed during the preparation phase (Obhi and Haggard 2004; Becchio et al. 2014; Viswanathan et al. 2019). In other words, the way the action was selected (freely chosen or instructed) should not influence the subsequent step of movement execution. Few studies have investigated the behavioral differences between freely chosen and instructed movements. Some, performed in humans, only found subtle differences in muscle activation, timing, or kinematic parameters of the movement (Obhi and Haggard 2004; Becchio et al. 2014; Viswanathan et al. 2019). A recent functional magnetic resonance imaging (fMRI) study found increased activation in the right inferior frontal opercular gyrus during the execution of freely chosen movements (Zapparoli et al. 2018). However, this study analyzed together the “what”, “when,” and “whether” components of intentional action during the execution phase. The brain region they identified is the conjunction part of these 3 modalities of free choice and may not be representative of the cerebral network underlying the execution of freely selected action. Other studies in nonhuman primates found that movement-related motor cortex activity did not differ between internally generated and externally cued movements that were associated with similar physical reaches (Lara, Cunningham, et al. 2018a; Lara, Ehsayed, et al. 2018b).

There is evidence suggesting that the network monitoring the congruence between the intentional content of our actions and their outcome should be enhanced during the execution of freely chosen as compared to instructed movements. According to the “forward model,” a computational model of motor control, a copy of the motor command (called the “efference copy”) is generated during movement preparation and is used to predict the sensory consequences of the movement. It is then sent to brain regions that compare these predictions with the sensory feedback generated by the movement during the execution phase (Wolpert et al. 1995; Haggard and Whitford 2004; Haggard 2008; Seghezzi et al. 2019). The parietal cortex and the cerebellum could be these “comparators” since they both represent sensorimotor interfaces integrating multisensory inputs and the efference copy (Wolpert et al. 1998; Desmurget and Grafton 2000; Blakemore and Sirigu 2003; Haggard and Whitford 2004; Jeannerod 2009; Haggard 2017; Seghezzi et al. 2019). The “forward model” is involved in different processes of movement execution: for rapid online correction of movements, for sensory attenuation, but also for the sense of agency (Miall et al. 1993; Wolpert et al. 1998; Desmurget and Grafton 2000; Synofzik et al. 2008; Haggard 2017; Dogge et al. 2019; Seghezzi et al. 2019). The sense of agency refers to the subjective feeling of being the author of our own actions (Haggard 2017). The sense of agency is usually divided in 2 distinct steps. The first one is referring to the low-level, nonconceptual, implicit feeling of control over an action, without relationship to any conscious thought and known as the “feeling of agency.” The second one is referring to the explicit judgment of being the source of the action outcome, also known as ‘judgment of agency’ or explicit agency. According to the “comparator model” of agency, the implicit “feeling of agency” relies on the comparison between the efference copy and the sensory feedback generated by the movement and could thus involve the cerebellum and the parietal cortex (Synofzik et al. 2008; Haggard 2017). Although the feeling of agency is also involved in instructed movements, it was recently shown that it is enhanced when the movement is freely chosen (Borhani et al. 2017; Haggard 2017; Barlas et al. 2018; Villa et al. 2020). We thus hypothesize that the “forward model network” responsible for the comparison between the intentional content of our actions and their outcome, in particular the parieto-cerebellar network, should be more recruited during the execution of freely chosen as compared to instructed movements.

Our goal was to clarify whether the modality of action selection (freely chosen or instructed) during movement preparation influences the brain network underlying the execution phase. We used an event-related fMRI design involving 20 healthy volunteers who performed a delayed response task. During the delay period, participants had to prepare a right-hand movement or a bimanual movement. The selection between these 2 possibilities was either freely chosen or instructed by an external cue. During the execution phase following the “Go” signal, the participants had to execute the prepared movement. This procedure allowed us to dissociate action selection, which occurs during the delay period, from the execution phase, including the reaction time (RT) and the movement itself. First, in the activation analysis, we compared the execution phase of freely chosen and instructed movements. Second, we used connectivity analysis (psychophysiological interaction [PPI]) to study the inter-regional covariation of key regions during the execution phase, with a special focus on the PPC and the cerebellum, 2 key structures of the forward model network.

Material and Methods

Subjects and Experimental Groups

Functional MRI data of freely chosen movements presented here were acquired simultaneously with motor preparation data of externally driven movements (Welniaz et al. 2019). The period of data acquisition ranged from 2013 to 2015. Twenty right-handed healthy volunteers (10 men and 10 women) aged from 20 to 64 years (mean age = 37.4 ± 2.58 years old) were recruited for the protocol. All the subjects were right-handed as assessed by the Edinburgh Inventory (Oldfield 1971). Because the current study was based on data that had already been acquired and because we had no a priori hypothesis on the effect size, we did not perform a statistical power analysis for the sample size. All the participants gave their written informed consent and the protocol was approved by the Ile-de-France 6 ethics committee (2013-A00616-39).

Organization of the Protocol

The experiment was described in a previous work focused on the motor preparation phase and on the effect of SMA stimulation (Welniaz et al. 2019), where data about the free choice condition and motor execution phase were not explored. Each healthy volunteer came for 2 visits. On each visit, the fMRI protocol (described below) was performed before and after real or sham stimulation of the SMA. The minimal interval between 2 visits was 4 weeks, to allow complete washout of the SMA stimulation effects. In the present study, we did not study the effects of SMA stimulation. However, in order to reach a sufficient number of trials in each condition for the event-related fMRI analysis (see below), we used the data collected during these 2 visits. The analyses were performed on the fMRI data that were acquired “before” the stimulation of the SMA during each visit. For each subject, the datasets were analyzed as repeated measures during 2 different visits (see Statistical Analysis).

Behavioral Paradigm

To study motor selection, we used a previously described delayed-response task (Welniaz et al. 2019). A first visual cue (S1) informed the subjects to respond with the right hand alone or with both hands (instructed condition), or to choose freely between these 2 possibilities (free choice condition, Fig. 1). To allow significant power for MRI data analysis, participants were asked to balance their choices in the free choice condition to have 50% of unimanual movements and 50% of bimanual movements. Following S1 presentation, the subjects had to prepare the movement but to remain motionless. A second cue (S2) instructed the subjects either to react (Go) or to withhold the prepared movement (NoGo). In Go trials, the subjects had to tap the finger motor sequence 2-4-3 (2: index finger, 3: middle finger, 4: ring finger) with the right hand alone or with both hands in a mirrored fashion on a keyboard compatible with the magnetic environment (one keyboard for each hand) as fast and precisely as possible after S2. The second cue (S2) was a Go signal in 75% of the cases and a NoGo signal in 25% of the cases. The introduction of “NoGo” trials allowed the attention level to be maintained while minimizing anticipatory responses. Following S2, the subjects had 3 s to respond before the next inter-trial interval. The time interval between S1 and S2 ranged between 1.5 and 2.5 s (mean centered on 2 s, jitter of ± 0.5 s, uniform distribution), and the inter-trial interval ranged

between 3 and 5 s (mean centered on 4 s, jitter of ± 1 s, uniform distribution). This experimental design allowed us to dissociate: 1) the preparation phase or delay period, between S1 and S2, when participants were motionless but were preparing the movement according to S1; 2) the execution phase, between the Go signal (S2) and the end of the subject movement that was determined by the last key press on the keyboard (Fig. 1). The average duration of a trial was 9 s, which was sufficient to avoid a significant contribution of the blood oxygen level-dependent response during motor execution to the delay period of the next trial. The order of conditions was randomized between runs and participants. Participants were familiarized with the task before the first fMRI recording. They were trained during 20 trials outside of the scanner.

Data Acquisition and Procedure

Behavioral Data

Four conditions were analyzed: instructed unimanual right-hand movements, instructed bimanual movements, freely chosen unimanual right-hand movements, and freely chosen bimanual movements. Motor errors (missed or wrong key presses, anticipated key presses before S2 occurrence) were recorded, and the error rate (number of motor errors/total number of trial) was calculated for each condition. The average RT (first key press after S2 occurrence for unimanual movements, average of the first key press of each hand after S2 occurrence for bimanual movements) was calculated for each condition. The average time of the execution phase (that includes the RT and movement execution) was calculated as the time separating the “Go signal” from the last key press of the motor sequence. During the free-choice trials, we used the participant’s responses on the keyboard to distinguish unimanual from bimanual trials. To verify that the participants performed the motor task correctly, and in particular to check that they remained motionless during the delay period, their hand movements were video recorded within the MRI. The trials that were not performed properly (missed or wrong key presses, anticipated key presses before S2 occurrence) were excluded from the behavioral and fMRI analyses.

EMG Data

Electromyographic (EMG) activity was recorded during the task performance inside the MRI scanner in all participants. EMG was acquired using nonmagnetic surface electrodes (20 kOhm impedance) with BrainVision Recorder (BrainProducts, <http://www.brainproducts.com>) at a sampling frequency of 5 kHz. Electrodes were placed over the flexor digitorum profundus and extensor digitorum communis of the left and right forearms. EMG signals were amplified using BrainAmp ExG MR toolbox and filtered to remove MRI gradient artifacts using a sliding average calculation implemented on BrainVision Analyser 2. Data were downsampled at 100 Hz. Data were centered on the mean signal and rectified using matlab (R2017b, MathWorks, USA). We segmented the EMG epochs using a marker of each movement condition that was associated with the presentation of S2 (Go signal) and the remaining 4 s after this marker. For each trial, the EMG envelope was calculated using a sliding window average (matlab function “movmean,” length = 10). For each participant and each condition, the mean EMG envelope was calculated averaging the 12 trials per run. The EMG onset was the first value of the mean EMG envelope that was higher than the threshold (15% of the maximal EMG amplitude) after

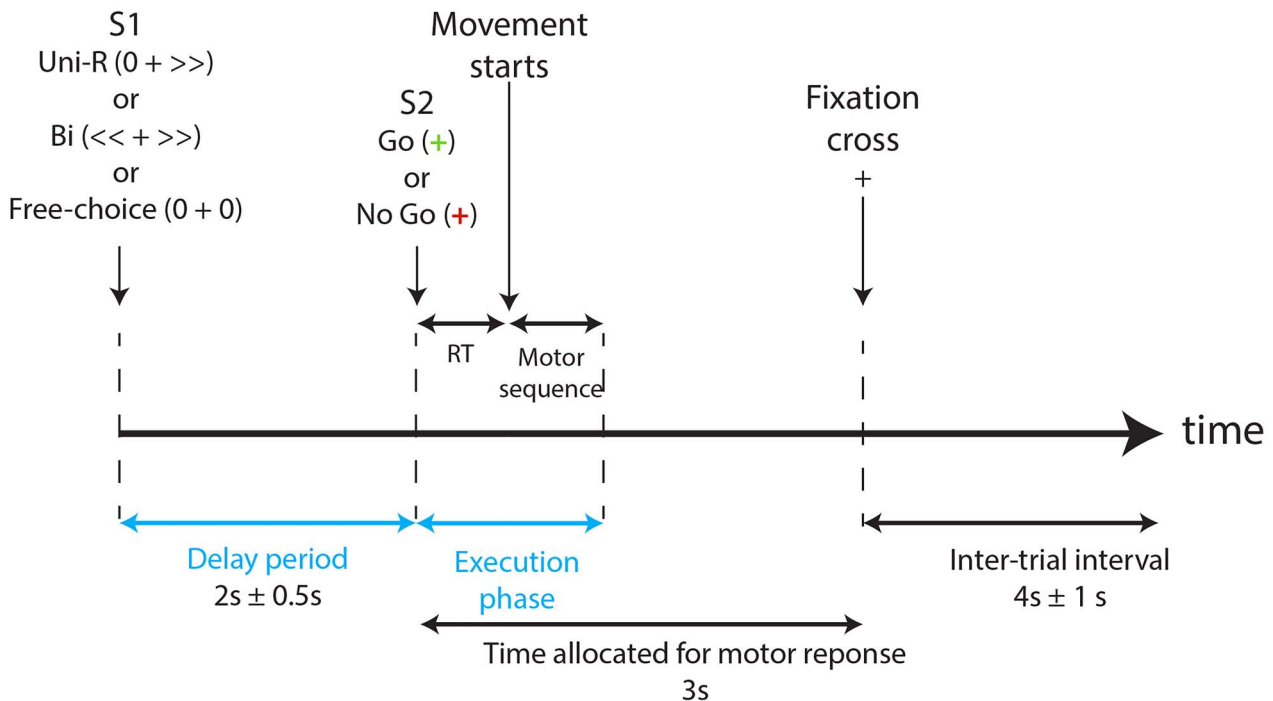


Figure 1. Organization of a trial in the delayed response task. The temporal windows used for fMRI analysis are represented in light blue: delay period and execution phase (that encompasses the RT and the movement execution itself). During the delay period, the subject had to prepare the forthcoming movement (right hand movement or bimanual movement) that was either instructed or freely chosen depending on S1. After the “Go” signal (S2), the subject had to execute the prepared movement. This procedure allowed us to separate action selection (that occurs during the delay period) from the execution phase. Uni-R, unimanual right hand movement; Bi, bimanual movement.

the task marker. The EMG offset was the first value of the mean EMG envelope that was below the same threshold after the point of maximal EMG amplitude (see example in Fig. 2). EMG duration was the difference between the offset value and the onset value. The area under the curve between the onset and the offset was calculated using the matlab function “trapz” and further called EMG amplitude.

Magnetic Resonance Imaging

The MRI device was a Siemens 3T MAGNETOM Verio with a 32-channel head coil. Echo planar images were acquired by multi-band imaging (time echo=30 ms, time repetition=1.31 s, flip angle=69°, voxel size=2 × 2 × 2 mm³, 60 slices, MB factor=4). The participants performed the task previously described, with the 2 keyboards placed on their upper thighs. During each of the 2 visits, participants performed 3 runs, each run comprising 12 trials with the instructed unimanual condition, 12 trials with the Instructed unimanual condition, 12 trials of the free-choice condition (the participants had to balance their choices between unimanual and bimanual movements), and 12 NoGo trials. The trials that were not performed properly were excluded from the fMRI analysis, so that for each of the 2 visits, the maximum number of trials available for the fMRI analysis was 36 (12 × 3) for the instructed unimanual condition, 36 for the instructed bimanual conditions, 18 (6 × 3) for the freely chosen unimanual condition, and 18 for the freely chosen bimanual condition. Regarding the free-choice condition, the repetition of the protocol during the second visit allowed us to reach the consensus minimal number of trials required for event-related fMRI analysis (30 trials) (Petersen and Dubis 2012; Soares et al.

2016). Images were preprocessed using SPM12: We applied slice-timing and head movement corrections (which amplitude was evaluated with the calculation of framewise displacement [FD]; the data were discarded when FD > 1.5), normalization based on the anatomical image using DARTEL, and smoothed (Gaussian kernel, full-width at half-maximum=8 mm). The physiological toolbox (tapas) was used to individually extract nuisance covariates (white matter signal, cerebrospinal fluid signal, 24 derivatives of head movement parameters) for the statistical analyses.

Statistical Analysis

Behavioral Data

Statistical analysis of the behavioral data was performed with the software R and JASP. The following variables were studied for the behavioral analysis: RT, the error rate, and the duration of the execution phase. Before performing the analysis, we checked the normality of the data distribution by visualization of the data distribution with density plot, Q-Q plot, and with the Shapiro test. When data distribution was not normal (for the RT and error rate), we used a logarithmic transformation on the data to perform the analyses. We used 2 kinds of statistical analyses.

First, we performed a standard analysis of variance (ANOVA) using a 2 × 2 × 2 design with repeated measures (Session: visit 1, visit 2; Selection: free choice, instructed; and Movement: unimanual, bimanual). We report the F-value and the P-value for main effects and interactions (significance level at $P < 0.05$).

Second, we used Bayesian statistics. Indeed, it has been shown that Bayesian statistics—as compared to the standard

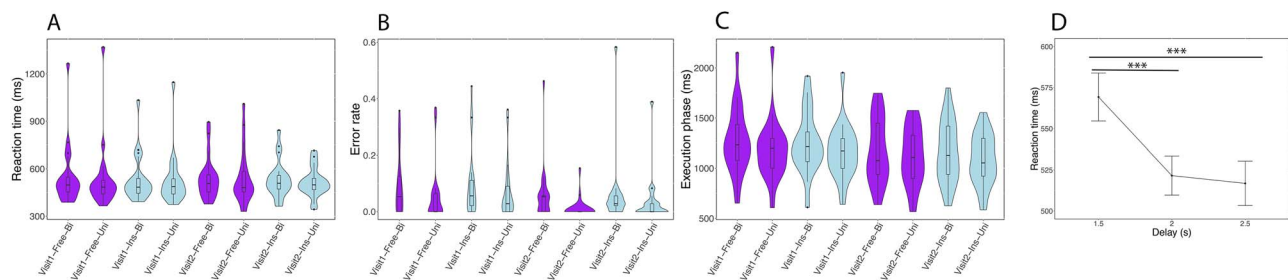


Figure 2. Behavioral performance in freely chosen and instructed movements. Violin plots representing the data of the $2 \times 2 \times 2$ repeated measures ANOVA (Session: visit 1, visit 2; Selection: free choice, instructed; and Movement: unimanual, bimanual) for the RT (A), the error rate (B), and the duration of the execution phase (C). (D) Plot showing the results of the $2 \times 3 \times 2 \times 2$ repeated measures ANOVA (Session: visit 1, visit 2; Delay: 1.5, 2, 2.5 s; Selection: free choice, instructed; and Movement: unimanual, bimanual) showing a significant effect of delay period duration on the reaction time. Ins-Uni, instructed unimanual movement; Ins-Bi, instructed bimanual movement; Free-Uni, freely chosen unimanual movement; Free-Bi, freely chosen bimanual movement. Light blue: Instructed movements. Purple: Freely chosen movements. ***: $p < 0.001$

framework of frequentist null-hypothesis significance testing—can provide evidence in favor of the null hypothesis. In other words, Bayesian statistics can provide evidence for an absence of difference (Keysers et al. 2020). With the software JASP, we conducted a Bayesian statistical analysis using the same $2 \times 2 \times 2$ repeated measures ANOVA design (Session: visit 1, visit 2; Selection: free choice, instructed; and Movement: unimanual, bimanual) with default priors. As recommended by Keysers et al., the effects are reported as the Bayes factor for the inclusion of a particular effect (BF_{incl}), calculated as the ratio between the likelihood of the data given the model versus the next simpler model without that effect. We also report the median and 95% confidence interval for each condition (Keysers et al. 2020). The interpretation of the Bayes factor was done as follows: For a given main effect or interaction, $BF > 10$ is strong evidence that there is a difference according to the considered main effect, $3 < BF < 10$ is moderate evidence for a difference, $1/3 < BF < 3$ is an absence of evidence, $1/10 < BF < 1/3$ is moderate evidence for an absence of difference, and $BF < 1/10$ is strong evidence for an absence of difference (Keysers et al. 2020).

In a last analysis, we aimed to verify that the subjects had prepared their movement during the delay period and not during the RT. To this end, we analyzed the RT relative to the distribution of the delay between the first cue and the Go signal. Indeed, according to a validated model (Trillenberg et al. 2000), each participant should predict the probability of a Go signal to occur according to the time already elapsed in the trial. In our study, the duration of the delay period was uniformly distributed across the following values: 1.5, 2, and 2.5 s. If the subjects prepared their movement during the delay period and were ready to move at the Go signal, the RT should be shorter for the longer durations of the delay period. Indeed, as time passes during a trial, the probability that a Go cue will be presented at the next possible delay increases (Trillenberg et al. 2000). Otherwise, if the subjects held online the first cue during the delay period and prepared the movement only after the Go cue, we would not expect any difference of RT according to the duration of the delay period. To disentangle these 2 possibilities, we performed a classical and a Bayesian $2 \times 3 \times 2 \times 2$ repeated measures ANOVA (Session: visit 1, visit 2; Delay: 1.5, 2, 2.5 s; Selection: free choice, instructed; and Movement: unimanual, bimanual) on the RT. For the classical ANOVA, we report the F -value and the P -value for main effects and interactions (significance level at $P < 0.05$). We checked the sphericity assumption, and if violated, we used the Greenhouse-Geisser sphericity correction. Post hoc tests were

corrected with the Bonferroni method. For the Bayesian ANOVA, we report the BF_{incl} and the 95% confidence interval for each condition.

EMG Data

Previous studies revealed that freely chosen as compared to instructed single-finger movements were associated with greater EMG activations (Obhi and Haggard 2004) and with a delayed timing of movement release (Viswanathan et al. 2019). We thus compared the amplitude and duration of the EMG activity in the index flexor and extensor between freely chosen and instructed movements without considering movement laterality. Individual values of EMG amplitude and duration were averaged over the 3 runs. We performed a classical and a Bayesian paired Wilcoxon test to isolate the Selection effect (free choice, instructed) on the EMG amplitude and duration. Since several tests were performed, P -values were corrected for multiple comparisons using a false discovery rate correction.

Functional Activation Data

Data were analyzed with statistical parametric mapping software (SPM12). Eight event-related conditions were defined. Four were related to the delay period, between S1 and S2 (Fig. 1): delay period of instructed unilateral movement; delay period of instructed bilateral movement; delay period of freely chosen unilateral movements; and delay period of freely chosen bilateral movements. Four were related to the execution phase, between S2 and the end of movement execution determined by the last key press on the keyboard (Fig. 1): execution of instructed unilateral movement; execution of instructed bilateral movement; execution of freely chosen unilateral movements; and execution of freely chosen bilateral movements. The execution phase thus encompasses both the RT (between S2 and movement onset) and the movement itself (between the first and the last key press on the keyboard). For the delay period, all the trials were analyzed, regardless of the nature of S2 (Go or NoGo). Regarding the execution phase, only the Go trials that were properly performed (see Behavioral Data) were included in the analysis. Using global linear models, we obtained 8 individual Z-score maps over the whole brain in each participant for the contrast of each condition versus implicit baseline. For the following group analyses, we defined flexible factorial designs to consider repeated measures. Contrast weights for the flexible factorial ANOVA were previously described (Glaescher

and Gitelman 2008). Age and gender of the participants were added as covariables of nuisance in all the second level analyses.

Several control analyses were carried out to ensure a correct interpretation of the results. The first control analysis verified the absence of significant differences in brain activations between the 2 visits. We conducted a $2 \times 2 \times 2 \times 2$ ANOVA (Session: visit 1, visit 2; Phase: delay period, execution phase; Selection: free choice, instructed; and Movement: unimanual, bimanual) and tested whether there was a main effect of session. The second control analysis ensured that we could separate the brain activity related to the delay period from the execution phase and that we could isolate the brain regions involved in freely chosen as compared to instructed movements. We defined a $2 \times 2 \times 2$ ANOVA (Phase: delay period, execution phase; Selection: free choice, instructed; Movement Type: unimanual, bimanual) and first looked at the main effect of Phase. We then focused on the main effect of Selection (averaged over the factor Phase) and the interaction effect of Phase \times Selection. In case of significant interaction effect, a good policy is to define 2 separate ANOVAs to compare the modalities of one factor, independently from the modalities of the second factor. Given the significance of the Phase \times Selection interaction effect, we defined 2 distinct 2×2 ANOVAs (Selection \times Movement), one during the “delay period” (third control analysis) and the other during the “execution phase” (main analysis). For each of these ANOVAs, we looked for the regions that were more activated during freely chosen movements (positive effect of free choice: free choice $>$ instructed). We also explored the opposite contrast (positive effect of instructed: instructed $>$ free choice). ANOVA results were considered significant at $P < 0.05$ with family-wise error (FWE) correction for multiple comparisons over the whole brain. The results are reported with an extent threshold of 10 voxels.

Connectivity Data

PPIs (Friston et al. 1997) display task-dependent changes in functional connectivity between seed regions of interest (seed ROIs) and the whole brain. This analysis was performed only for the execution phase. Seed ROIs were selected based on the results of the activation analysis, including masks of clusters that were more activated during the execution phase of freely chosen versus instructed movement. The main analysis was performed on 3 seed ROIs: the left PPC, the right PPC, and the left cerebellum Crus 1. We performed an exploratory PPI analysis on an additional seed ROI: the preSMA (see [Supplemental Material](#)). For each subject, the time course extracted from each seed ROI was a vector containing a single value (e.g., the mean activity in the mask) for each time point, corrected by a F contrast (effect of interest) to center the data. Inter-regional covariation was captured at the individual level by performing a linear regression, in which the activity in the seed region (Y), the contrast of interest (P), and the interaction between Y and P (PPI) were used as regressors. The task-dependent effect was determined by the contrast testing the positive effect of freely chosen and instructed movement separately. The task-dependent effect was evaluated separately for unimanual and bimanual conditions. The conditions that were not considered in the task-dependent effect were defined as standard regressors in the linear regression to model the variance. Positive effect of the PPI regressor was tested using a t -test at the individual level, considering individual contrasts of the freely chosen and instructed movement separately. These individual contrasts were submitted to the group analysis, which consisted of a 2×2

ANOVA (Selection \times Movement) for each of the seed ROI. In the main effect of Selection of the group analysis, the instructed trials were used as the control condition to remove signal related to the motor output. For the ANOVA analysis, we used a ROI-based correction approach: We made the hypothesis that a parieto-cerebellar network would show increased connectivity during the execution of freely chosen as compared to instructed movements. Thus, for the connectivity of the left and right PPC, we used a mask over the cerebellum, including the following bilateral regions in the aal coordinates on the wfu pickatlas: Cerebellum Crus 1, Cerebellum 3, Cerebellum 4_5, Cerebellum 6, Cerebellum 7b, Cerebellum 8, Cerebellum 9, Cerebellum 10, Vermis 1 2, Vermis 3, Vermis 4_5, Vermis 6, Vermis 7, Vermis 8, Vermis 9, and Vermis 10. For the connectivity of the cerebellum, we used a mask over the PPC, including the following bilateral regions in the aal coordinates on the wfu pickatlas: parietal superior, parietal inferior, and supramarginal. Contrasts were thresholded using pFTCE approach (Smith and Nichols 2009; Han et al. 2019), with FWE corrected threshold of $P < 0.05$.

Results

Behavioral Data

During the free choice condition, the average percentage of unimanual hand movement was 48.3%, showing that the participants followed the instruction to balance their choices between unimanual and bimanual movements.

To test the effect of the modality of selection (free choice or instructed movement) on the behavioral response, we performed a $2 \times 2 \times 2$ repeated measure ANOVA (Session: visit 1, visit 2; Selection: freely chosen, instructed; and Movement: unimanual, bimanual) on the RT, the error rate, and the duration of the execution phase.

We first used classical statistical analysis. We found that the RT, the error rate, and the duration of the execution phase were not significantly different between the first and second visits (no effect of Session: $F_{1,19} = 0.016$; $P = 0.9$ for the RT; $F_{1,19} = 2$; $P = 0.17$ for the error rate; $F_{1,19} = 3.16$; $P = 0.091$ for the duration of the execution phase; [Fig. 2](#)). The RT, the error rate, and the duration of the execution phase were not significantly different between instructed and freely chosen movements (no effect of Selection: $F_{1,19} = 1.12$; $P = 0.304$ for the RT; $F_{1,19} = 3.1$; $P = 0.09$ for the error rate; $F_{1,19} = 2.50$; $P = 0.13$ for the duration of the execution phase; [Fig. 2](#)). The RT was not significantly different between unimanual and bimanual movements (no effect of Movement: $F_{1,19} = 1.94$; $P = 0.18$; [Fig. 2](#)), but the error rate was increased during the execution of bimanual movements as compared to unimanual movement, during both instructed and freely chosen movements (effect of Movement: $F_{1,19} = 23$; $P < 0.001$; no movement \times selection interaction: $F_{1,19} = 3.08$; $P = 0.09$; [Fig. 2](#)). The duration of the execution phase was also increased during bimanual movements, during both instructed and freely chosen movements (effect of Movement: $F_{1,19} = 18.5$; $P < 0.001$; no movement \times selection interaction: $F_{1,19} = 0.28$; $P = 0.6$; [Fig. 2](#)).

We then used a Bayesian statistical approach on the same $2 \times 2 \times 2$ repeated measure ANOVA design. For the RT, there was evidence that there was no difference of RT according to the effect of Session, Selection, and Movements, as the Bayes factors were less than or close to 1/3 (effect of Session $BF_{incl} = 0.173$; effect of Selection $BF_{incl} = 0.242$; effect of Movement $BF_{incl} = 0.360$; [Supplemental Tables 1 and 2](#)) (Keyesers

et al. 2020). For the error rate, there was strong evidence that there was an effect of Session ($BF_{\text{incl}} = 19.2$) and Movement ($BF_{\text{incl}} = 9.3$). By contrast, there was evidence for an absence of difference according to the effect of Selection ($BF_{\text{incl}} = 0.25$; [Supplemental Tables 1 and 2](#)). Similarly, for the duration of the execution phase, there was strong evidence that there was an effect of Session ($BF_{\text{incl}} = 131$) and Movement ($BF_{\text{incl}} = 36$). By contrast, there was evidence for an absence of difference according to the effect of Selection ($BF_{\text{incl}} = 0.13$; [Supplemental Tables 1 and 2](#)). Overall, this Bayesian statistical approach allowed us to conclude that the RT, the error rate, and the duration of the execution phase were not different between freely chosen and instructed movements.

In the analysis considering the RT relative to the duration of the delay period, we performed a classical and a Bayesian $2 \times 3 \times 2 \times 2$ repeated measures ANOVA (Session: visit 1, visit 2; Delay: 1.5, 2, 2.5 s; Selection: free choice, instructed; and Movement: unimanual, bimanual) on the RT. In the classical ANOVA, we found no effect of Session ($F_{1,19} = 0.012$, $P = 0.91$), no effect of Selection ($F_{1,19} = 0.90$, $P = 0.35$), no effect of Movement ($F_{1,19} = 1.47$, $P = 0.24$) but a main effect of Delay period ($F_{1,19} = 30.15$, $P < 0.001$; [Fig. 2D](#)). We found no interaction effect (Session \times Delay period: $F_{1,19} = 1.002$, $P = 0.96$; Selection \times Delay period interaction: $F_{1,19} = 1.21$, $P = 0.31$; Movement \times Delay period: $F_{1,19} = 0.44$, $P = 0.63$). The post hoc analysis revealed a longer RT for the first delay (1.5 s) as compared to the second delay (2 s; $P < 0.001$) and to the third delay (2.5 s; $P < 0.001$), while there was no significant difference between the second and third delays ($P = 0.22$; [Fig. 2D](#)). The Bayesian analysis showed the same results. Evidence showed no difference of RT according to the effect of Session, Selection, and Movements, as the Bayes factors were less than 1/3 (effect of Session $BF_{\text{incl}} = 0.015$; effect of Selection $BF_{\text{incl}} = 0.027$; effect of Movement $BF_{\text{incl}} = 0.045$; [Fig. 2D](#); [Supplemental Tables 1 and 2](#)). By contrast, there was strong evidence for an effect of Delay ($BF_{\text{incl}} = 194\,599$; [Fig. 2D](#)). Post hoc tests revealed a longer RT for the first delay (1.5 s) as compared to the second delay (2 s; $BF_{\text{incl}} = 1.8 \times 10^7$) and to the third delay (2.5 s; $BF_{\text{incl}} = 1.6 \times 10^{10}$), while there was evidence for an absence of difference between the second and third delays ($BF_{\text{incl}} = 0.27$). Overall, these results provide evidence that the subjects had prepared their movement during the delay period and were ready to move at the Go signal.

EMG Analysis

Using both classical and Bayesian statistical analyses, we found evidence for a greater EMG activity and duration during freely chosen as compared to instructed movement (amplitude in the flexor muscle: $P = 0.004$, $BF_{10} = 122$; duration in the flexor muscle: $P = 0.028$, $BF_{10} = 5.7$; amplitude in the extensor muscle: $P = 0.012$, $BF_{10} = 16$; duration in the extensor muscle: $P = 0.042$, $BF_{10} = 2.8$; [Fig. 3](#)).

fMRI Activation Analysis

Our aim was to determine whether the brain network underlying action execution depends on whether the selection of the action was freely chosen or instructed during the delay period. We therefore conducted the following analyses: 1) characterization of the temporal windows used for the fMRI analysis; 2) control analyses; 3) the main analysis, which consisted of a 2×2 ANOVA (Selection: free choice, instructed; and Movement: unimanual, bimanual) during the execution phase of the movement.

Regarding the temporal windows used for the fMRI analysis, the mean duration of the delay period (between S1 and S2) was 2 s. The mean duration of the execution phase (between the Go signal and the end of movement execution, determined by the last key press on the keyboard) was 1.17 s ([Fig. 1](#)). On average, the duration of the motor sequence and of the RT represented 55% and 45% of the total duration of the execution phase, respectively ([Fig. 1](#)).

Control Analysis 1

The first control analysis verified the absence of significant differences in brain activations between the 2 visits using the $2 \times 2 \times 2 \times 2$ ANOVA (Session: visit 1, visit 2; phase: delay period, execution phase; selection: free choice, instructed; and movement: unimanual, bimanual). Indeed, the main effect of Session did not yield to any significant difference between visit 1 and visit 2. In the following ANOVAs, data from the 2 visits were entered as repeated measures but the Session factor was no longer tested in the flexible factorial designs.

Control Analysis 2

We performed a $2 \times 2 \times 2$ ANOVA (Phase: delay period, execution phase; Selection: free choice, instructed; and Movement: unimanual, bimanual). The main effect of Phase showed that for a large number of brain regions, their level of activity was significantly modulated between the delay period and the execution phase. Post hoc t-tests identified a set of brain regions on both sides of the brain that was more activated during the delay period (delay period $>$ execution phase), including the occipital cortex, the SMA, the precentral cortex, and the insula ([Supplemental Table 3](#); [Supplemental Fig. 1](#)). As expected, the opposite contrast (execution phase $>$ delay period) showed increased activation in several regions known to be involved in motor execution: the primary motor cortex, the primary somatosensory cortex, the striatum, and the cerebellum ([Supplemental Table 3](#); [Supplemental Fig. 1](#)). The main effect of Selection showed that for a large number of brain regions, their level of activity was significantly modulated between the free choice and instructed conditions, regardless of the movement phase (delay period or execution phase). For the positive effect of free choice (free choice $>$ instructed), we found increased activation during freely chosen as compared to instructed movements in the following regions: the preSMA, the ACC, the middle and inferior frontal gyrus, the inferior parietal cortex, the cerebellum, the middle temporal cortex and the insula, as well as the right precuneus ([Supplemental Table 3](#), [Supplemental Fig. 2A](#)). Regarding the opposite contrast (instructed $>$ free choice), we found increased activation in the left and right cuneus and precuneus as well as the left inferior frontal cortex, the frontal median orbital cortex, the left hippocampus, the left middle occipital cortex, the olfactory cortex, and the right angular cortex ([Supplemental Table 3](#), [Supplemental Fig. 2A](#)). The interaction Phase \times Selection identified the brain regions which modulation of activity between freely chosen and instructed movements was different during the delay period and the execution phase ([Supplemental Table 3](#), [Supplemental Fig. 2B](#)): the left and right hippocampus, cuneus, and precuneus were more activated in the instructed condition as compared to the free choice condition during the execution phase, while these regions were more activated by freely chosen movements during the delay period.

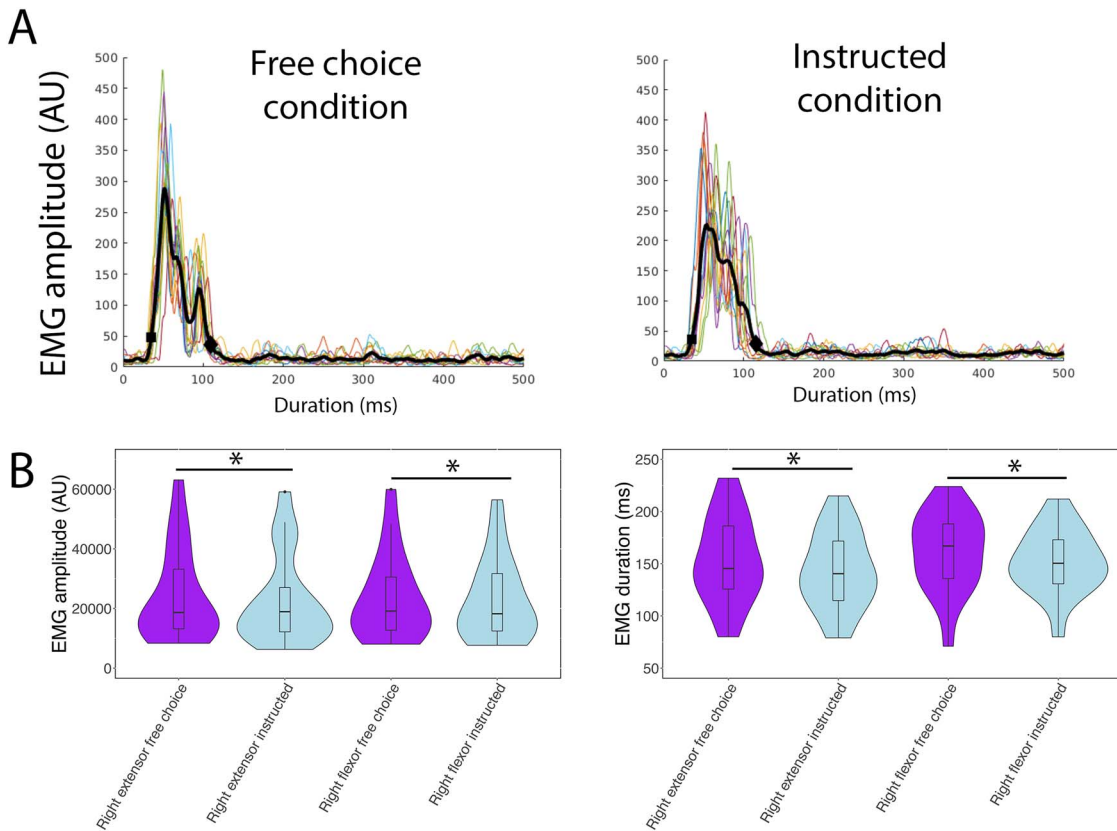


Figure 3. Electromyographic recordings during the performance of freely chosen and instructed movements. (A) EMG mean envelope (black plot) and EMG envelopes of 12 trials (color plots) during the instructed (right panel) and freely chosen movement (left panel) for a representative subject. EMG onset (black diamond) automatically thresholded at 15% of the maximal amplitude. (B) Violin plots showing the effects of condition on EMG duration (EMG onset time – EMG offset time) and EMG amplitude (area under the curve between EMG onset and EMG offset). *: $p < 0.05$.

Control Analysis 3

The 2×2 ANOVAs (Selection \times Movement) for the delay period showed that freely chosen as compared to instructed movements were associated with greater activation in different brain areas: the left preSMA, the left precuneus, the left and right inferior parietal cortices, the right middle cingulum, the left ACC, the right and left middle frontal gyrus, and the left insula (Supplemental Table 4A, Supplemental Fig. 3). The opposite contrast (positive effect of instructed: instructed $>$ free choice) yielded no results during the delay period.

Main Analysis

We focused on the execution phase using a 2×2 ANOVA (Selection: free choice, instructed; and Movement: unimanual, bimanual). We identified the brain regions that were more activated during the execution of freely chosen as compared to instructed movements (positive effect of free choice: free choice $>$ instructed): the bilateral inferior parietal cortices, the left middle orbital frontal cortex, the left cerebellum Crus 1, areas of the medial wall (the right dorsal preSMA and bilateral medial frontal sulcus), the left middle temporal cortex, and areas of the right frontal lobe (Table 1; Fig. 4). Results of the opposite contrast (positive effect of instructed: instructed $>$ free choice) showed an increase of activation in the left inferior frontal lobe, the left occipital cortex, and a bilateral network including the hippocampus and the cuneus (Supplemental Table 4B, Supplemental Fig. 3). The main effect of Movement showed

an increased activation of the right precentral cortex and of the left cerebellum during bimanual as compared to right-hand movements (Supplemental Table 4B). The Selection \times Movement interaction displayed no significant result.

fMRI Connectivity Analysis

For the connectivity analysis, our aim was to identify the brain network recruited during the execution phase of freely chosen as compared to instructed movements. Using PPI, we studied the connectivity of different ROIs (seed ROI) that were chosen among the results of our activation analysis, showing increased activation in the free choice condition (free choice $>$ instructed) during the execution phase. These seed ROIs included the right and left inferior PPC and the left cerebellum Crus 1. According to the forward model of motor control, a parieto-cerebellar network is thought to be involved in comparing the expected motor outcome with the actual sensory feedback (Blakemore and Sirigu 2003; Synofzik et al. 2008), and we expected this network to be more recruited during the execution of freely chosen as compared to instructed movements.

Using an ROI-driven approach, we looked whether the left and right PPC had increased connectivity with the cerebellum during the execution of freely chosen as compared to instructed movements. We showed that the right PPC had increased connectivity with the left cerebellum 6, the right cerebellum 4, 5, Crus 1, and Crus 2 during the execution of freely chosen as

Table 1 Comparison of blood oxygen level-dependent response between freely chosen and instructed movements during the execution phase

Contrast/anatomical location	MNI coordinates	kE	Z score (F score)
Positive effect of free choice (free choice > instructed)			
Right superior parietal	38–64 54	496	6.51
Left superior parietal	–36 –64 54	214	6.37
Left frontal middle orbital	–44 52–8	174	6.37
Left cerebellum Crus 1	–42 –72 –32	15	5.96
Right preSMA	4 28 62	45	5.42
Right middle frontal	44 24 44	27	5.36
Right middle frontal	36 62–2	61	5.34
Left medial frontal superior	0 42 30	31	5.32
Left middle temporal	–64 –30 –12	12	5.4
Right frontal superior	20 56 32	16	5.25
Right middle frontal	32 18 60	18	5.17

Note: MNI coordinates were derived from a 2×2 ANOVA selection (free choice; instructed) \times movement (unimanual right; bimanual). Contrasts were thresholded at a FWE corrected threshold of $P < 0.05$ over the whole brain, with a minimum cluster size of 10 voxels. MNI, Montreal Neurological Institute.

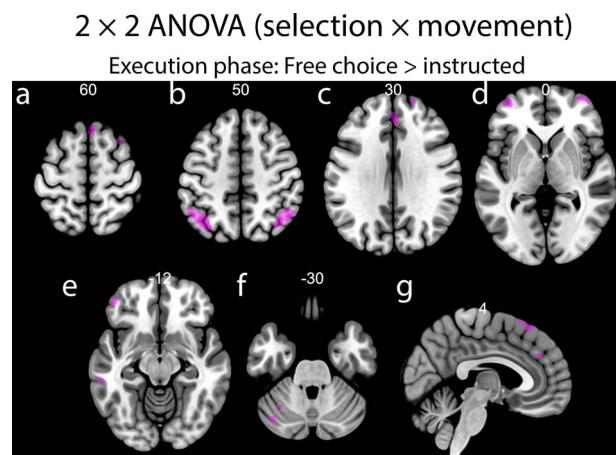


Figure 4. Brain regions underlying the execution phase of freely chosen movements. Anatomical location of the brain areas more activated during freely chosen as compared to instructed movements (free choice > instructed) during the execution phase of the movement: the bilateral inferior parietal cortices (B), the left middle orbital frontal cortex (E), the left cerebellum Crus 1 (F), areas of the medial wall including the right dorsal preSMA and bilateral medial frontal sulcus (A, C, G), the left middle temporal cortex (E), and areas of the right frontal lobe (A, C, D). (A–F) Axial views of the brain. (G) Sagittal view of the human brain. The numbers above the axial views represent the z-axis and the numbers above the sagittal views represent the x-axis. All ANOVA results were considered significant at $P < 0.05$ with FWE correction for multiple comparisons over the whole brain.

compared to instructed movements (free choice > instructed; Table 2; Fig. 5). The opposite contrast (instructed > free choice) yielded no results. The same analysis performed on the left PPC resulted in no significant result.

Conversely, we looked whether the left cerebellum Crus 1 showed increased connectivity with either PPC: this analysis yielded no significant result.

We performed an exploratory PPI analysis on an additional seed ROI: the preSMA (see Supplemental Material for details). We found increased connectivity of the preSMA with the SMA proper, the left and right posterior parietal cortices, and the right temporo-parieto-occipital junction (TPJ) during the execution of freely chosen as compared to instructed movements (Supplemental Table 5, Supplemental Fig. 4).

Discussion

Using fMRI activation and connectivity analyses, we identified a brain network that was more involved during the execution phase of freely chosen as compared to instructed movements. This demonstrates that the degree of engagement of this network during action execution depends on how the movement was selected during the delay period (freely chosen or instructed). This network included the preSMA, the PPC, and the cerebellum, which are known to contribute to volition, to the formation of motor plans but also to sensory integration. We suggest that the execution of freely chosen movements elicits functional interaction in a network that monitors the congruence between the intentional content of our actions and their outcomes. Our findings provide further evidence supporting the forward model of motor control.

In a control procedure, we isolated brain areas involved in the free choice versus instructed condition regardless of the movement phase (delay period or execution). We found a large set of bilateral brain regions: the PPC, the SMA and preSMA, the ACC, the middle and inferior frontal gyrus, the cerebellum, the middle temporal cortex, the precuneus, and the insula. All these regions were previously linked to the “what component” of freely chosen movements (Deiber et al. 1991; Lau, Rogers, Ramnani, et al. 2004b; Forstmann et al. 2006; van Eimeren et al. 2006; Mueller et al. 2007; Krieghoff 2009; Hoffstaedter et al. 2013; Ariani et al. 2015; Zapparoli et al. 2017, 2018), confirming the validity of our experimental setup. We then compared freely chosen and instructed movements during the delay period and execution phase separately. Many of the previous fMRI studies addressing this topic did not use an event-related design, so that movement preparation and execution could not be disentangled in the analysis (Deiber et al. 1991; Lau, Rogers, Ramnani, et al. 2004b; Forstmann et al. 2006; van Eimeren et al. 2006; Mueller et al. 2007; Filevich et al. 2013; Hoffstaedter et al. 2013), while other studies focused on the delay period (Krieghoff 2009; Ariani et al. 2015; Zapparoli et al. 2018). Using activation analyses, we identified a set of brain regions that were more activated during the execution phase of freely chosen as compared to instructed movements: the bilateral inferior parietal cortices, the left middle orbital frontal cortex, the left cerebellum Crus 1, areas of the medial wall (the right dorsal preSMA and bilateral medial frontal sulcus), the left middle temporal cortex, and areas of the right frontal lobe. This demonstrates that the modality of

Table 2 Comparison of the functional connectivity of the right PPC between freely chosen and instructed movements during the execution phase

Contrast/Anatomical location	MNI Coordinates	kE	Z score (F score)
Positive effect of free choice (free choice > instructed)			
Left cerebellum 6	-42 -50 -28	5	4.51
Right cerebellum 4-5	22-74 -20	19	4.50
Right cerebellum Crus 2	26-78 -36	5	4.49
Right cerebellum Crus 1	24-74 -34	3	4.43
Right cerebellum Crus 1	32-76 -34	1	4.43
Right cerebellum Crus 1	40-62 -30	3	4.41
Right cerebellum Crus 1	22-78 -30	1	4.37
Right cerebellum Crus 1	20-76 -32	1	4.35

Note: MNI coordinates were derived from a 2×2 ANOVA selection (free choice; instructed) \times movement (unimanual right; bimanual). Contrasts were thresholded using pFTCE approach, with FWE corrected threshold of $P < 0.05$ over the mask including the voxels of the entire cerebellum. MNI, Montreal Neurological Institute.

PPI 2×2 ANOVA (selection \times movement)

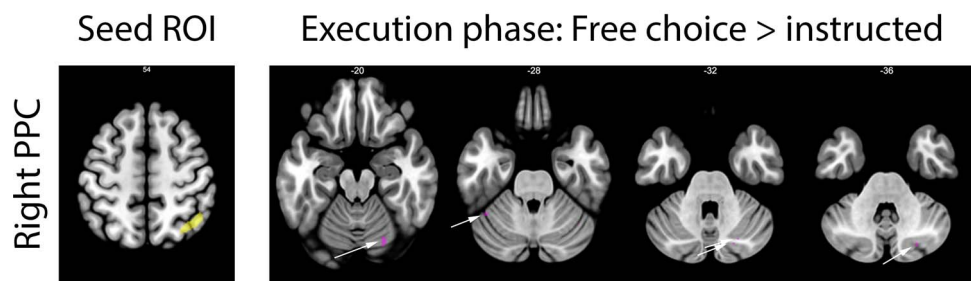


Figure 5. Increased parieto-cerebellar connectivity during the execution phase of freely chosen movements. Three ROIs (seed ROIs) obtained in the activation analysis were used for the PPI model: the left and right PPC and the left cerebellum Crus 1. The results are displayed only for the right PPC, as the analysis of the other seed ROIs resulted in no significant result. The left panel shows the location of the seed ROI used in the connectivity analysis. The right panel shows the anatomical location of the cerebellar regions that showed increased connectivity with the seed ROI during the execution phase of freely chosen movements (free choice > instructed; purple, white arrows). Contrasts were thresholded using pFTCE approach, with FWE corrected threshold of $P < 0.05$ over the mask including the voxels of the entire cerebellum.

action selection (freely chosen or instructed) does not only influence the brain network involved in the delay period, but also the network involved during the subsequent execution of the movement.

Few studies analyzed separately the preparation and execution of freely chosen movements (Krieghoff 2009; Zapparoli et al. 2018). They found increased activation in the middle frontal gyrus, the inferior frontal gyrus, and the inferior parietal lobule during the execution of freely chosen movements. While these regions are consistent with our results, the aforementioned studies did not find any activation in the cerebellum or in the preSMA as we did. This discrepancy between our results and the previous findings can be explained by different methodological approaches. The study of Zapparoli et al. analyzed together the “what”, “when,” and “whether” components of intentional action during the execution phase. The brain region they identified may be the conjunction of these 3 modalities of free choice, whereas our results are restricted to the “what” component of intention. The different temporal windows used by Krieghoff and collaborators could explain the difference between their results and ours. Indeed, they focused on a 1-s temporal window starting at movement onset. Our temporal window encompassed both the RT (from the Go signal to the beginning of the movement) and the movement time, to capture a global “execution time.” Such a temporal window

may represent a limitation. The RT is classically considered as a preparatory phase for the ongoing movement (Crammond and Kalaska 2000; Haith et al. 2016; Lara, Elsayed, et al. 2018b). So the question arises whether the differences that we observe between the execution phases of freely chosen versus instructed movements are related to differences in a selection process still ongoing during the RT or to differences in the movement phase per se. First, our behavioral analysis provided strong evidence that movement preparation was completed at the end of the delay period. A previous model showed that depending on the distribution of the delay between the first cue and the Go signal, the participant predict the probability of a Go signal to occur according to the time already elapsed in the trial (Trillenberg et al. 2000). When the delay is uniformly distributed (such as in our study), the RT should be shorter for the longer durations of the delay period: As time passes during a trial, the probability that a Go cue will be presented at the next possible delay increases (Trillenberg et al. 2000). Our results showed that the RT was significantly shorter for the longer delays, indicating that the subjects had completed the preparation of the movement by the end of the delay period. Furthermore, in nonhuman primates, it was shown that in delayed response tasks, prior information about the forthcoming movement elicits neuronal activity during the delay period that normally occurs during the RT of simple RT tasks (where a single cue indicates at the same

time the movement to perform and the Go signal) (Crammond and Kalaska 2000). Thus, information processing that occurs after the “Go” signal is modified in delayed response tasks, and in particular, a neuronal population in the dorsal premotor cortex (PMd) consistently showed a reduced discharge during the RT as compared to the delay period (Crammond and Kalaska 2000). In the same line of thinking, transcranial magnetic stimulation experiments repeatedly showed that there is a decreased excitability of the corticospinal tract to the target muscle during the delay period, which represents an inhibition of the selected effector. That same inhibition is observed during the RT when the subject had to select their action after the Go signal (choice RT task) (Duque and Ivry 2009; Duque et al. 2017). This suggests that action selection occurs during the delay period in delayed response tasks, while it occurs during the RT in choice RT tasks. Lastly, the idea that the RT represents the preparatory processes needed before movement execution has been recently challenged. It was suggested that movement preparation and initiation are independent processes (Haith et al. 2016). Taken together, this supports the view that in delayed response tasks, action selection is completed at the end of the delay period as opposed to other experimental paradigms. It is thus unlikely that the differences we observe during the execution phase of freely chosen versus instructed movements could be caused by the process of action selection spreading from the delay period to the RT. However, the transition between preparatory and execution processes appears to be gradual rather than sharp (Chen and Hallett 1999) and seems to occur during the RT, making a clear cut between them difficult to realize (Lara, Elsayed, et al. 2018b). In keeping with this, the RT and movement execution are not dissociable in most fMRI designs using 2 stimuli for delayed response tasks (one for the delay period, the other for the execution). Indeed, the RT and the execution per se always occur in the same order and are less than 500 ms apart, which can be considered as co-occurrence and prevents the separability of these 2 elements in the deconvolution analysis. In any case, using Bayesian statistical analysis, we showed that there was no difference of RT between freely chosen and instructed movements in our study: The RT period similarly affects the execution phase of both conditions. The only resulting difference likely results from the preceding selection modality.

We focused our functional connectivity analysis on the PPC and the cerebellum, acknowledging that these structures are critical parts of the forward model network (Wolpert et al. 1998; Desmurget and Grafton 2000; Blakemore and Sirigu 2003; Haggard and Whitford 2004; Seghezzi et al. 2019). Electrophysiology experiments have revealed an increased connectivity between the PPC and the PMd during a free search task and during sensorimotor mapping of sequences executed with the fingers (Pesaran et al. 2008; Karabanov et al. 2012). Here, we identified a parieto-cerebellar network involved in the execution of freely chosen movements, as revealed by the increased connectivity of the right PPC with the cerebellum.

What is the functional significance of the brain network we identified during the execution of freely chosen movements? In other words, what are the behavioral and cognitive differences between the execution of freely chosen and instructed movements that could explain the recruitment of this specific network? It has long been assumed that the execution phase of the movement was limited to the activation of primary motor regions and that the underlying cortical network should not differ whether the movement was freely chosen or instructed (Obhi

and Haggard 2004; Becchio et al. 2014; Viswanathan et al. 2019). In nonhuman primates, it was recently shown that the neural state of the SMA during movement execution is dependent on the context, that is, on whether the movement was internally generated or externally triggered during the preparation phase (Lara, Cunningham, et al. 2018a). In addition, the execution of freely chosen and instructed movements in humans slightly differs with regard to behavioral parameters. An EMG study found that freely choosing the timing of action (“when” component) is associated with greater muscle activation (Obhi and Haggard 2004). There is also evidence that the execution of internally and externally generated movements differ according to subtle kinematic parameters: The total duration of the movement is increased and the time to maximal grip aperture is delayed in freely chosen movements (for the “what”, “when,” and “whether” components) (Becchio et al. 2014). In a task involving a simple movement (pressing a button) that was either instructed or freely chosen (“what component”), the button release was delayed in the free choice condition, and this was associated a delayed β -rebound over the contralateral sensory motor cortex (Viswanathan et al. 2019). In our task involving a simple-finger sequence and focused on the “what component” of intention, the recording of the EMG signal in the flexor and extensor muscles of the fingers revealed a longer duration and increased amplitude of the EMG activity in freely chosen as compared to instructed movements, replicating prior findings (Obhi and Haggard 2004; Becchio et al. 2014; Viswanathan et al. 2019). It appears that the subtle EMG differences we observed between freely chosen and instructed movements had no repercussion on the engagement of the cortical motor areas. The primary motor cortex encodes the force amplitude (Dettmers et al. 1995; Wexler et al. 1997) and is activated during the release of hand force (Toma et al. 1999). Thus, it seems unlikely that the differences in brain activity observed between the 2 conditions could be caused by the subtle kinematic and timing differences in the execution of the movement. Instead, they are likely related to other types of brain events occurring at execution time.

One possibility to explain this behavioral difference during the execution of freely chosen movements is that these movements are associated with different motor preparation processes compared to instructed movements (Obhi and Haggard 2004). Due to our study design, we present several arguments indicating that the selection processes were performed during the delay period, while the execution period was associated with the performance of the already prepared action. A second possibility would be that freely chosen movements are executed using a different mode of control than instructed movement. In a previous study that required the subjects to press a button, freely chosen and instructed movements both ended up with beta rebound (Viswanathan et al. 2019). However, the beta rebound was linked to the push movement in the instructed condition, while it was linked to the release movement in the freely chosen condition. The authors suggest that different movement-related information is considered during freely chosen movement, with a mode of touch-governed movement control. Altogether, we suggest that what affects the parieto-cerebellar network during freely chosen movement is the processing of the movement’s outcome, that is, somatosensory and proprioceptive feedback.

An interesting hypothesis is that execution of freely chosen movements is associated with a greater involvement of the network that monitors the congruence between the intentional content of our actions and their outcomes. The “forward model,”

a computational model of motor control, provides a framework for such a process. According to this model, a copy of the motor command (called the “efference copy”) that represents the intentional content of the forthcoming action is generated during the preparation phase and is used to predict the sensory consequences of the movement. It is sent to brain regions called “comparators” where it is a posteriori compared with the sensory feedback generated by the movement (Miall et al. 1993; Wolpert et al. 1995; Haggard 2008; Jeannerod 2009). The “forward model” is involved in different processes of movement execution: for rapid online correction of movements, for sensory attenuation, and also for the implicit “feeling of agency” (Desmurget and Grafton 2000; Synofzik et al. 2008; Haggard 2017; Dogge et al. 2019; Seghezzi et al. 2019; Tanaka et al. 2020). Concerning the neuroanatomy of the “forward model,” several brain regions have been identified. On the one hand, the SMA, preSMA, and the PPC play a critical role in the subjective feeling of free choice or “conscious intention” (Lau, Rogers, Haggard, et al. 2004a; Desmurget et al. 2009; Desmurget and Sirigu 2012), and they have been repeatedly associated with freely chosen movements and motor planning (Nachev et al. 2008; Zapparoli et al. 2018). On the other hand, the parietal cortex and the cerebellum both integrate multisensory inputs, and it was proposed that the efference copy could originate from the SMA while the parietal cortex and the cerebellum could be “comparators” by monitoring the congruence between the efference copy and the sensory feedbacks generated by the movement (Miall et al. 1993; Wolpert et al. 1998; Desmurget and Grafton 2000; Blakemore and Sirigu 2003; Haggard and Whitford 2004; Waszak et al. 2012; Haggard 2019; Welniarz et al. 2021). Accordingly, a mismatch between the initial motor intention and the perceived movement outcome triggers activations in the PPC, the preSMA, the cerebellum, the temporal lobe, and in particular the temporoparietal junction (Fink et al. 1999; Nahab et al. 2011; Sperduti et al. 2011; Haggard 2017; Seghezzi et al. 2019; van Kemenade et al. 2019; Zito et al. 2020). In addition, a recent study showed that the activity in the preSMA, the PPC, and the cerebellum correlated with the degree of intentional binding, a behavioral parameter used to evaluate the implicit feeling of agency (Zapparoli et al. 2020). Because the implicit feeling of agency is enhanced when the movement is freely chosen as compared to instructed (Borhani et al. 2017; Barlas et al. 2018; Villa et al. 2020), a greater recruitment of these “feeling of agency” areas—and in particular the parieto-cerebellar network—was expected during the execution of freely chosen as compared to instructed movements.

Our results are consistent with this hypothesis. First, in the activation analysis, we found greater activation of the preSMA, the bilateral PPC, and the cerebellum during the execution of freely chosen as compared to instructed movements. Second, we found that the execution of freely chosen movements was associated with an increased functional connectivity between the right PPC and the cerebellum. Third, an exploratory connectivity analysis showed that preSMA had an increase of coupling with the SMA proper, the left and right posterior parietal cortices, and the right TPJ (see [Supplemental Material](#)). This last result suggests the implication of feedforward mechanisms from motor preparation to detect possible mismatch between the intentional content and the action results. We thus suggest that the execution of freely chosen movements is associated with a greater monitoring of the congruence between the intentional content of our actions and their outcomes, resulting in an increased activation and connectivity of a network including

the preSMA, the PPC, and the cerebellum. Of note, the right but not the left PPC showed increased connectivity with the cerebellum. This fits with the results of a meta-analysis showing that the right but not the left PPC is involved in intentional action and self-agency, conjointly (Seghezzi et al. 2019). Involvement of this network during action execution may be important to coherently appreciate self-chosen movements, integrating the “what” component of intentionality and the action results.

The main limitation of the study is that we did not measure any of the behavioral parameters that have been associated with the “forward model,” such as the sense of agency or sensory attenuation. An additional limitation is related to the “free choice” experimental paradigm that we used, which is reductive as compared to the situations we experience in daily-life. In tasks requiring the participants to perform a sequence of “free choices” where the different outcomes are equivalent, the brain activity preceding and following the subject’s responses is not solely related to free action selection and execution. Brain activity is also influenced by the regularity of passed choices: The subjects monitor their past behavior to update their set of responses and implement transient and arbitrary response rules, such as the inhibition of repetition (Baddeley et al. 1998; Bunge 2004; Zhang and Rowe 2015; Phillips et al. 2018). These processes would reduce the randomness (entropy) of responses (Phillips et al. 2018). Some of the brain activations we observed during the execution of freely chosen movements may have been related to the monitoring of past responses to balance the free choices between unimanual and bimanual movements. Such a bias is intrinsic to the type of experimental paradigm we used. In both MEG and fMRI studies, it was shown that the entropy of freely chosen responses was negatively correlated to the activity in the prefrontal cortex (Zhang and Rowe 2015; Phillips et al. 2018). This rather suggests that the monitoring of past responses was performed by other areas than the parieto-cerebellar network. In addition, RT during the execution phase depends on the duration of the delay period, suggesting the absence of additional cognitive process during the execution of freely chosen movements. Another limitation is that the design of our study did not allow us to determine whether the lateralization of the brain activation and connectivity we observed were related to the laterality of the hand movement. In our study, we did not find any Selection × Movement interaction, meaning that the brain activation and connectivity patterns were independent from the movement type (unimanual right or bimanual). However, in right-handed subjects, the dominant (left) hemisphere initiates both bimanual movements and unimanual right-hand movements. By contrast, movements of the nondominant hand elicit activations in a different network (Haaland and Harrington 1996; Solodkin et al. 2001; Haaland 2006; Walsh et al. 2008). Thus, because we did not test for unimanual left-hand movements, we cannot conclude whether the brain activation and connectivity pattern we observed were related or not to movement laterality.

In conclusion, it has been known that a freely chosen movement compared to the same commanded movement is stronger and has a greater sense of agency. The findings here show that these features are likely due to a larger feedforward signal giving knowledge of the expected outcome of the movement. Freely chosen movements, having a strong sense of being voluntary, also develop a correlative sense of responsibility recognized by the individual and society.

Supplementary Material

Supplementary material can be found at *Cerebral Cortex* online.

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References

- Ariani G, Wurm MF, Lingnau A. 2015. Decoding internally and externally driven movement plans. *J Neurosci.* 35:14160–14171.
- Baddeley A, Emslie H, Kolodny J, Duncan J. 1998. Random generation and the executive control of working memory. *Q J Exp Psychol Sect A.* 51:819–852.
- Barlas Z, Hockley WE, Obhi SS. 2018. Effects of free choice and outcome valence on the sense of agency: evidence from measures of intentional binding and feelings of control. *Exp Brain Res.* 236:129–139.
- Becchio C, Zanatto D, Straulino E, Cavallo A, Sartori G, Castiello U. 2014. The kinematic signature of voluntary actions. *Neuropsychologia.* 64:169–175.
- Blakemore S-J, Sirigu A. 2003. Action prediction in the cerebellum and in the parietal lobe. *Exp Brain Res.* 153:239–245.
- Borhani K, Beck B, Haggard P. 2017. Choosing, doing, and controlling: implicit sense of agency over somatosensory events. *Psychol Sci.* 28:882–893.
- Brass M, Haggard P. 2008. The what, when, whether model of intentional action. *Neuroscientist.* 14:319–325.
- Bunge SA. 2004. How we use rules to select actions: a review of evidence from cognitive neuroscience. *Cogn Affect Behav Neurosci.* 4:564–579.
- Chen R, Hallett M. 1999. The time course of changes in motor cortex excitability associated with voluntary movement. *Can J Neurol Sci J Can Sci Neurol.* 26:163–169.
- Crammond DJ, Kalaska JF. 2000. Prior information in motor and premotor cortex: activity during the delay period and effect on pre-movement activity. *J Neurophysiol.* 84:986–1005.
- Cui H, Andersen RA. 2007. Posterior parietal cortex encodes autonomously selected motor plans. *Neuron.* 56:552–559.
- Cunnington R, Windischberger C, Deecke L, Moser E. 2002. The preparation and execution of self-initiated and externally-triggered movement: a study of event-related fMRI. *Neuroimage.* 15:373–385.
- Deiber MP, Ibanez V, Sadato N, Hallett M. 1996. Cerebral structures participating in motor preparation in humans: a positron emission tomography study. *J Neurophysiol.* 75:233–247.
- Deiber M-P, Passingham RE, Colebatch JG, Friston KJ, Nixon PD, Frackowiak RSJ. 1991. Cortical areas and the selection of movement: a study with positron emission tomography. *Exp Brain Res.* 84:393–402.
- Desmurget M, Grafton S. 2000. Forward modeling allows feedback control for fast reaching movements. *Trends Cogn Sci.* 4:423–431.
- Desmurget M, Reilly KT, Richard N, Szathmari A, Mottolese C, Sirigu A. 2009. Movement intention after parietal cortex stimulation in humans. *Science.* 324:811–813.
- Desmurget M, Sirigu A. 2012. Conscious motor intention emerges in the inferior parietal lobule. *Curr Opin Neurobiol.* 22:1004–1011.
- Dettmers C, Fink GR, Lemon RN, Stephan KM, Passingham RE, Silbersweig D, Holmes A, Ridding MC, Brooks DJ, Frackowiak RS. 1995. Relation between cerebral activity and force in the motor areas of the human brain. *J Neurophysiol.* 74:802–815.
- Dogge M, Custers R, Aarts H. 2019. Moving forward: on the limits of motor-based forward models. *Trends Cogn Sci.* 23:743–753.
- Duque J, Greenhouse I, Labruna L, Ivry RB. 2017. Physiological markers of motor inhibition during human behavior. *Trends Neurosci.* 40:219–236.
- Duque J, Ivry RB. 2009. Role of corticospinal suppression during motor preparation. *Cereb Cortex N Y N 1991.* 19:2013–2024.
- Filevich E, Vanneste P, Brass M, Fias W, Haggard P, Kühn S. 2013. Brain correlates of subjective freedom of choice. *Conscious Cogn.* 22:1271–1284.
- Fink GR, Marshall JC, Halligan PW, Frith CD, Driver J, Frackowiak RSJ, Dolan RJ. 1999. The neural consequences of conflict between intention and the senses. *Brain.* 122:497–512.
- Forstmann BU, Brass M, Koch I, von Cramon DY. 2006. Voluntary selection of task sets revealed by functional magnetic resonance imaging. *J Cogn Neurosci.* 18:388–398.
- Friston KJ, Buechel C, Fink GR, Morris J, Rolls E, Dolan RJ. 1997. Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage.* 6:218–229.
- Glaescher J, Gitelman D. 2008. Contrast weights in flexible factorial design with multiple groups of subjects. *SPM@JISCMail.* AC.UK) Sml, editor, 1–12.
- Haaland KY. 2006. Left hemisphere dominance for movement. *Clin Neuropsychol.* 20:609–622.
- Haaland KY, Harrington DL. 1996. Hemispheric asymmetry of movement. *Curr Opin Neurobiol.* 6:796–800.
- Haggard P. 2008. Human volition: towards a neuroscience of will. *Nat Rev Neurosci.* 9:934–946.
- Haggard P. 2017. Sense of agency in the human brain. *Nat Rev Neurosci.* 18:196–207.
- Haggard P. 2019. The neurocognitive bases of human volition. *Annu Rev Psychol.* 70:9–28.
- Haggard P, Whitford B. 2004. Supplementary motor area provides an efferent signal for sensory suppression. *Cogn Brain Res.* 19:52–58.
- Haith AM, Pakpoor J, Krakauer JW. 2016. Independence of movement preparation and movement initiation. *J Neurosci.* 36:3007–3015.
- Hallett M. 2016. Physiology of free will. *Ann Neurol.* 80:5–12.
- Han H, Glenn AL, Dawson KJ. 2019. Evaluating alternative correction methods for multiple comparison in functional neuroimaging research. *Brain Sci.* 9.
- Hoffstaedter F, Grefkes C, Zilles K, Eickhoff SB. 2013. The “What” and “When” of self-initiated movements. *Cereb Cortex.* 23:520–530.
- Jeannerod M. 2009. The sense of agency and its disturbances in schizophrenia: a reappraisal. *Exp Brain Res.* 192:527–532.
- Karabanov A, Jin S-H, Joutsen A, Poston B, Aizen J, Ellenstein A, Hallett M. 2012. Timing-dependent modulation of the posterior parietal cortex–primary motor cortex pathway by sensorimotor training. *J Neurophysiol.* 107:3190–3199.

- Keyesers C, Gazzola V, Wagenmakers E-J. 2020. Using Bayes factor hypothesis testing in neuroscience to establish evidence of absence. *Nat Neurosci.* 23:788–799.
- Kriehoff V. 2009. Dissociating what and when of intentional actions. *Front Hum Neurosci.* 3.
- Kurata K, Wise SP. 1988. Premotor and supplementary motor cortex in rhesus monkeys: neuronal activity during externally- and internally-instructed motor tasks. *Exp Brain Res.* 72:237–248.
- Lara AH, Cunningham JP, Churchland MM. 2018a. Different population dynamics in the supplementary motor area and motor cortex during reaching. *Nat Commun.* 9.
- Lara AH, Elsayed GF, Zimnik AJ, Cunningham JP, Churchland MM. 2018b. Conservation of preparatory neural events in monkey motor cortex regardless of how movement is initiated. *Elife.* 7.
- Lau HC, Rogers RD, Haggard P, Passingham RE. 2004a. Attention to intention. *Science.* 303:1208–1210.
- Lau HC, Rogers RD, Ramnani N, Passingham RE. 2004b. Willed action and attention to the selection of action. *Neuroimage.* 21:1407–1415.
- Miall RC, Weir DJ, Wolpert DM, Stein JF. 1993. Is the cerebellum a Smith predictor? *J Mot Behav.* 25:203–216.
- Mueller VA, Brass M, Waszak F, Prinz W. 2007. The role of the preSMA and the rostral cingulate zone in internally selected actions. *Neuroimage.* 37:1354–1361.
- Nachev P, Kennard C, Husain M. 2008. Functional role of the supplementary and pre-supplementary motor areas. *Nat Rev Neurosci.* 9:856–869.
- Nahab FB, Kundu P, Gallea C, Kakareka J, Pursley R, Pohida T, Milettta N, Friedman J, Hallett M. 2011. The neural processes underlying self-agency. *Cereb Cortex N Y N* 1991. 21:48–55.
- Obhi SS, Haggard P. 2004. Internally generated and externally triggered actions are physically distinct and independently controlled. *Exp Brain Res.* 156:518–523.
- Okano K, Tanji J. 1987. Neuronal activities in the primate motor fields of the agranular frontal cortex preceding visually triggered and self-paced movement. *Exp Brain Res.* 66:155–166.
- Oldfield RC. 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia.* 9:97–113.
- Passingham RE. 2007. Two cortical systems for directing movement. In: Bock G, O'Connor M, Marsh J, editors. *Novartis Foundation Symposia*. Chichester: John Wiley & Sons, Ltd., pp. 151–170.
- Pesaran B, Nelson MJ, Andersen RA. 2008. Free choice activates a decision circuit between frontal and parietal cortex. *Nature.* 453:406–409.
- Petersen SE, Dubis JW. 2012. The mixed block/event-related design. *Neuroimage.* 62:1177–1184.
- Phillips HN, Cope TE, Hughes LE, Zhang J, Rowe JB. 2018. Monitoring the past and choosing the future: the prefrontal cortical influences on voluntary action. *Sci Rep.* 8:7247.
- Rasmussen T, Penfield W. 1947. The human sensorimotor cortex as studied by electrical stimulation. *Fed Proc.* 6:184.
- Romo R, Schultz W. 1987. Neuronal activity preceding self-initiated or externally timed arm movements in area 6 of monkey cortex. *Exp Brain Res.* 67:656–662.
- Seghezzi S, Zirone E, Paulesu E, Zapparoli L. 2019. The brain in (willed) action: a meta-analytical comparison of imaging studies on motor intentionality and sense of agency. *Front Psychol.* 10.
- Smith S, Nichols T. 2009. Threshold-free cluster enhancement: addressing problems of smoothing, threshold dependence and localisation in cluster inference. *Neuroimage.* 44:83–98.
- Soares JM, Magalhães R, Moreira PS, Sousa A, Ganz E, Sampaio A, Alves V, Marques P, Sousa N. 2016. A Hitchhiker's guide to functional magnetic resonance imaging. *Front Neurosci.* 10.
- Solodkin A, Hlustik P, Noll DC, Small SL. 2001. Lateralization of motor circuits and handedness during finger movements. *Eur J Neurol.* 8:425–434.
- Sperduti M, Delaveau P, Fossati P, Nadel J. 2011. Different brain structures related to self- and external-agency attribution: a brief review and meta-analysis. *Brain Struct Funct.* 216:151–157.
- Synofzik M, Vosgerau G, Newen A. 2008. Beyond the comparator model: a multifactorial two-step account of agency. *Conscious Cogn.* 17:219–239.
- Tanaka H, Ishikawa T, Lee J, Kakei S. 2020. The cerebro-cerebellum as a locus of forward model: a review. *Front Syst Neurosci.* 14.
- Toma K, Honda M, Hanakawa T, Okada T, Fukuyama H, Ikeda A, Nishizawa S, Konishi J, Shibasaki H. 1999. Activities of the primary and supplementary motor areas increase in preparation and execution of voluntary muscle relaxation: an event-related fMRI study. *J Neurosci.* 19:3527–3534.
- Trillenber P, Verleger R, Wascher E, Wauschkuhn B, Wessel K. 2000. CNV and temporal uncertainty with 'ageing' and 'non-ageing' S1–S2 intervals. *Clin Neurophysiol.* 111:1216–1226.
- van Eimeren T, Wolbers T, Münchau A, Büchel C, Weiller C, Roman Siebner H. 2006. Implementation of visuospatial cues in response selection. *Neuroimage.* 29:286–294.
- van Kemenade BM, Arikan BE, Podranski K, Steinsträter O, Kircher T, Straube B. 2019. Distinct roles for the cerebellum, angular gyrus, and middle temporal gyrus in action–feedback monitoring. *Cereb Cortex.* 29:1520–1531.
- Villa R, Tidoni E, Porciello G, Aglioti SM. 2020. Freedom to act enhances the sense of agency, while movement and goal-related prediction errors reduce it. *Psychol Res.* 85:987–1004.
- Viswanathan S, Wang BA, Abdollahi RO, Daun S, Grefkes C, Fink GR. 2019. Freely chosen and instructed actions are terminated by different neural mechanisms revealed by kinematics-informed EEG. *Neuroimage.* 188:26–42.
- Walsh RR, Small SL, Chen EE, Solodkin A. 2008. Network activation during bimanual movements in humans. *Neuroimage.* 43:540–553.
- Waszak F, Cardoso-Leite P, Hughes G. 2012. Action effect anticipation: neurophysiological basis and functional consequences. *Neurosci Biobehav Rev.* 36:943–959.
- Waszak F, Wascher E, Keller P, Koch I, Aschersleben G, Rosenbaum DA, Prinz W. 2005. Intention-based and stimulus-based mechanisms in action selection. *Exp Brain Res.* 162:346–356.
- Welniarz Q, Gallea C, Lamy J-C, Méneret A, Popa T, Valabregue R, Béranger B, Brochard V, Flamand-Roze C, Trouillard O et al. 2019. The supplementary motor area modulates interhemispheric interactions during movement preparation. *Hum Brain Mapp.* 40:2125–2142.
- Welniarz Q, Worbe Y, Gallea C. 2021. The forward model: a unifying theory for the role of the cerebellum in motor control and sense of agency. *Front Syst Neurosci.* 15:644059.
- Wexler BE, Fulbright RK, Lacadie CM, Skudlarski P, Kelz MB, Constable RT, Gore JC. 1997. An fMRI study of the human cortical

- motor system response to increasing functional demands. *Magn Reson Imaging*. 15:385–396.
- Wolpert D, Ghahramani Z, Jordan M. 1995. An internal model for sensorimotor integration. *Science*. 269:1880–1882.
- Wolpert DM, Miall RC, Kawato M. 1998. Internal models in the cerebellum. *Trends Cogn Sci*. 2:338–347.
- Zapparoli L, Seghezzi S, Paulesu E. 2017. The what, the when, and the whether of intentional action in the brain: a meta-analytical review. *Front Hum Neurosci*. 11.
- Zapparoli L, Seghezzi S, Scifo P, Zerbi A, Banfi G, Tettamanti M, Paulesu E. 2018. Dissecting the neurofunctional bases of intentional action. *Proc Natl Acad Sci*. 115:7440–7445.
- Zapparoli L, Seghezzi S, Zirone E, Guidali G, Tettamanti M, Banfi G, Bolognini N, Paulesu E. 2020. How the effects of actions become our own. *Sci Adv*. 6.
- Zhang J, Rowe JB. 2015. The neural signature of information regularity in temporally extended event sequences. *Neuroimage*. 107:266–276.
- Zito GA, Wiest R, Aybek S. 2020. Neural correlates of sense of agency in motor control: a neuroimaging meta-analysis. *PLoS One*. 15:e0234321.