


RESEARCH ARTICLE

Neural correlates of proprioceptive upper limb position matching

Francesca Marini¹  | Jacopo Zenzeri¹ | Valentina Pippo¹ | Pietro Morasso¹ | Claudio Campus²

¹Department of Robotics, Brain and Cognitive Sciences, Istituto Italiano di Tecnologia, Genoa, Italy

²U-VIP Unit for Visually Impaired People, Istituto Italiano di Tecnologia, Genoa, Italy

Correspondence

Francesca Marini, Department of Robotics, Brain and Cognitive Sciences, Istituto Italiano di Tecnologia, Genoa, Italy.

Email: francesca.marini17@gmail.com

Abstract

Proprioceptive information allows humans to perform smooth coordinated movements by constantly updating one's mind with knowledge of the position of one's limbs in space. How this information is combined with other sensory modalities and centrally processed to form conscious perceptions of limb position remains relatively unknown. What has proven even more elusive is pinpointing the contribution of proprioception in cortical activity related to motion. This study addresses these gaps by examining electrocortical dynamics while participants performed an upper limb position matching task in two conditions, namely with proprioceptive feedback or with both visual and proprioceptive feedback. Specifically, we evaluated the reduction of the electroencephalographic power (desynchronization) in the μ frequency band (8–12 Hz), which is known to characterize the neural activation associated with motor control and behavior. We observed a stronger desynchronization in the left motor and somatosensory areas, contralateral to the moving limb while, parietal and occipital regions, identifying association and visual areas, respectively, exhibited a similar activation level in the two hemispheres. Pertaining to the influence of the two experimental conditions it affected only movement's offset, and precisely we found that when matching movements are performed relying only on proprioceptive information, a lower cortical activity is entailed. This effect was strongest in the visual and association areas, while there was a minor effect in the hand motor and somatosensory areas.

KEYWORDS

EEG, ERSP, proprioception, robotic assessment, μ band desynchronization

1 | INTRODUCTION

People depend on signals coming from their moving bodies to interact with the space around them and respond in a meaningful way to challenging circumstances. Knowledge about position of the limbs and trunk, called position sense, is provided largely by sensations arising in proprioceptors, the sensory receptors located in muscles, tendons, joints, and the inner ear that respond to movement and position (Proske & Gandevia, 2012). The information they provide allows us to

perceive our body in space (Bastian, 1887; Sherrington, 1907) and it plays a crucial role in interacting with the external world by guiding movement planning and by constantly updating the central nervous system regarding limb and joint positions (Sober & Sabes, 2003; van Beers, Sittig, & van der Gon, 1999). Indeed, the loss or elimination of proprioception due to neurological disorders and brain injuries results in severe motor deficits (Sainburg, Ghilardi, Poizner, & Ghez, 1995). Given its importance, proprioception has always received significant attention from the field of human neurophysiology (Proske &

Gandevia, 2009; Tsay, Giummarra, Allen, & Proske, 2016) and, in recent years, the topic has received additional impetus owing to advances in robotic technologies that have allowed experts to develop reliable, accurate, and objective tests (Dukelow et al., 2010; Marini, Ferrantino, & Zenzeri, 2018; Marini, Squeri, Morasso, Konczak, & Masia, 2016; Rinderknecht, Popp, Lamercy, & Gassert, 2016).

Such expansion of knowledge has led to recognition of the importance of a deeper investigation of proprioception to improve the comprehension of human physiology and motor control, and also to move forward in developing understanding of how to help the brain recover from an injury (Schabrun & Hillier, 2009; Sullivan & Hedman, 2008) and how to create proprioceptive senses in prosthetics devices (Raspovic et al., 2014; Tabot, Kim, Winberry, & Bensmaia, 2015).

Despite a number of neurophysiological, behavioral, and clinical studies on the roles of proprioception, the corresponding neural correlates have received little attention and relatively little is still known about the central processing of this perceptual modality in the brain.

Functional neuroimaging studies have attempted to determine the brain areas responsible for proprioceptive processing, but there remains disagreement as to the specific brain regions involved (Kenzie, Ben-Shabat, Lamp, Dukelow, & Carey, 2018). Moreover, due to the difficulty of uncoupling proprioception from motor control (Scott, 2012), most of the functional magnetic resonance imaging (fMRI) studies had to limit the study of proprioceptive mechanisms to the perception of limb displacement and position in the absence of movement execution. Specifically, these studies identified the specific brain areas related to limb proprioception during illusory movements elicited by vibrotactile stimulation (Goble et al., 2011; Goble et al., 2012; Naito et al., 2007). Though interesting, such findings cannot reliably measure limb position, as the vibrotactile stimulus elicits an illusion of movement, likely due to activation of the muscle spindles, without any actual limb motion (Han, Waddington, Adams, Anson, & Liu, 2016; Kenzie et al., 2018).

It is only recently that fMRI has been used to study position sense during actual limb motion but with evidences limited to the ankle joint (Iandolo et al., 2018) in healthy participants or the upper limb in post-stroke subjects (Kenzie, Findlater, Pittman, Goodyear, & Dukelow, 2019). We also believe that complementing such information with the functional evidence coming from electrophysiological techniques could enrich the fMRI studies dramatically. Unfortunately such potential synergy has been very limited so far: electrophysiological studies focused mainly on the cortical representation of passive motion (Alary et al., 1998; Alegre et al., 2002; Seiss et al., 2002; Szurhaj et al., 2003), or exclusively aimed to contrast patterns of brain activation between disabled individuals and healthy control subjects, without considering aspects related to limb movement perception (Restuccia et al., 2003; Seiss, Praamstra, Hesse, & Rickards, 2003). Besides, several studies investigated the activations associated with visual reaching movements (Bernier, Burle, Hasbroucq, & Blouin, 2009) but, in contrast, experts have given little attention to understanding the cascade of neural processes related to matching movements toward a target when visual feedback is absent. In this sense, there are still gaps to be filled in our knowledge of the patterns of neural activity related to

somatosensory perception during active limb movements, and to date, an electrophysiological analysis of the neural correlates of position matching is missing.

Considering the general framework, the main goal of the present study was to develop an experimental protocol combining electroencephalographic (EEG) activity and a robot-based proprioceptive test based on reproduction of unseen hand location that is commonly used to measure proprioceptive hand-target and joint position sense (Goble, 2010; Jones, Fiehler, & Henriques, 2012). The specific objective was to compare patterns of neural activity between active movements performed with and without visual feedback under visuoproprioceptive (VP) and proprioceptive (P) conditions, respectively.

A comprehensive study of upper limb position matching, including its neural correlates during an active matching task, could provide further insight into understanding how the human brain processes limb position sense information. It may also yield information as to whether there are differences with respect to the visual processing of active movements.

In pursuit of this aim, we collected EEG activity data from a group of healthy individuals while they performed a robotic position-matching task in which they replicated a target position with the upper limb (Goble, 2010). We compared between VP and P conditions the event-related spectral perturbation (ERSP) (Makeig, 1993; Makeig, Debener, Onton, & Delorme, 2004) in the μ band, whose oscillations have been used to characterize the neural dynamics associated with motor control and behavior (McFarland, Miner, Vaughan, & Wolpaw, 2000; Niedermeyer, 1997; Pfurtscheller & Aranibar, 1979).

2 | METHODS

2.1 | Participants

Twenty-three healthy participants (age 24.3 ± 6.4 years, 11 males, 12 females) took part in this study. The study has been carried out in accordance with the Declaration of Helsinki, which protects research subjects, and the local ethical committee of Liguria Region approved it (n. 222REG2015, "Upper limb sensorimotor learning studies using robotic interfaces"). Subjects gave their informed consent, had normal or corrected-to-normal vision and no history of neurological or psychiatric disorders. The Edinburgh Handedness Inventory (Oldfield, 1971) test assessed subjects' handedness, showing that all participants were right-hand dominant. The experiment was carried out at the Motor Learning, Assistive and Rehabilitation Robotics Laboratory of the Istituto Italiano di Tecnologia (Genoa, Italy).

2.2 | Experimental setup

The robotic workstation employed in the experiments is based on a haptic, planar manipulandum with 2° of freedom (Casadio, Sanguineti, Morasso, & Arrichiello, 2006). The robot has a large planar workspace (80×40 cm ellipse) and a rigid structure with two direct drive brushless motors that provide full back-drivability, low intrinsic mechanical impedance, and an effective isotropy index at the end-effector.

The robot can measure the trajectory of the hand with high-resolution (<0.1 mm) and is smoothly impedance-controlled to generate continuous force fields with a magnitude ranging from fractions of 1 N up to 50 N. The control architecture is based on the real-time operating system RT-Lab and includes three nested control loops: (a) an inner 16 kHz current loop; (b) an intermediate 1 kHz impedance control loop; and (c) an outer 100 Hz loop for visual display and data storage.

Subjects sat in a comfortable chair, grasping the handle of the robot with the right hand and facing the computer monitor that displayed the trial-based paradigm (Figure 1a).

2.3 | Experimental protocol

We recorded brain activity while subjects performed (with their right hand) an ipsilateral Position Matching task, typically employed for assessing proprioceptive acuity (Goble, 2010). In this test, subjects performed center-out matching movements on a horizontal plane at shoulder level. The reference position was in the midline at a distance of about 20 cm from the chest. Figure 1b shows the timeline of this test and four phases composed each trial: (a) passive displacement (operated by the robot) of the hand to a target position; (b) holding time (3 s) when the subject was asked to memorize the position of the hand, followed by the first passive return to the reference starting position; (c) active matching movement performed by the subject to the previously memorized position. Instruction to the subject was to reproduce (i.e., match) the previously experienced unseen hand position. In this phase, the robot was idle and only used for measuring the kinematics of the matching movement. The last phase, (d) consisted in the passive return to the reference starting position.

Four auditory cues lead subjects through the task: a first cue marked the beginning of the passive movement toward the target and (1,024 Hz frequency beep lasting 45 ms), at its end, another cue signaled that the target had been reached (512 Hz, 45 ms). Later, an auditory cue indicated to the subject that the active matching movement could begin (1,024 Hz, 45 ms) and, finally, a last cue sounded when the subject reached the target position (512 Hz, 45 ms).

The study employed five different proprioceptive targets, which were randomly chosen trial by trial to avoid a mere repetition of the same matching movement and prevent learning: these targets were located at a 25 cm distance from the reference with a small angular shift among them (-5° , -2.5° , 0° , $+2.5^\circ$, $+5^\circ$). The passive displacements the robot performed were implemented with a smooth, minimum jerk profile.

Two different experimental conditions were used in the different trials: a VP condition and a P condition. The VP condition was characterized by the fact that, during the whole trial, subjects received visual feedback of the hand position that consisted of a yellow circular cursor (1 cm) on the visual screen without any visual display of the target position. In this condition, the subject received continuous sensory feedback regarding the hand position through visual and proprioceptive modalities. In the P condition, subjects did not receive any visual feedback and they receive specific instructions to exclusively rely and focus on the proprioceptive feedback from their arm and hand. In both conditions, vision of the arm was occluded through a board for the duration of the experiment and subjects did not receive any feedback about their performance in the task.

The experimental protocol consisted of six target sets of 30 trials, for each one of the two conditions and the entire experiment of $30(\text{trial}) \times 6(\text{target set}) \times 2(\text{conditions}) = 360$ trials lasted about 2 hr. The two conditions were randomized among target sets. Subjects also received a chance to rest and refocus between target sets.

2.4 | Electrophysiological data recording and preprocessing

EEG activity was recorded continuously from 64 Ag–AgCl active electrodes (Biosemi Active 2 EEG System) embedded in an elastic cap in accordance with the extended 10/20 system. Preamplifiers in each electrode were used to lessen the induced noise between the electrode and the amplification/digitization system (BioSemi ActiveTwo, BioSemi B.V. Amsterdam), thus allowing high electrode impedances. Electrode offsets were kept below 35 mV and a first-order analog

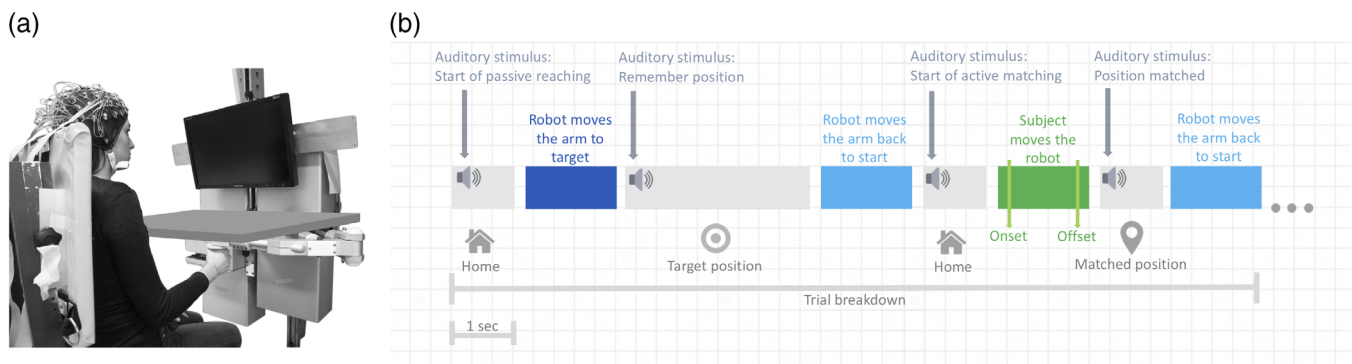


FIGURE 1 (a) A typical subject performing the position matching task with the robotic device and a board occluding vision of the arm; (b) Trial timeline. In each trial, the robot passively moved the arm toward a target position and then repositioned it to the starting position. The subject then actively moved the arm in an attempt to replicate the target position (movement's onset and offset triggered at 2 cm/s velocity threshold). Once the active movement completed, the robot passively repositioned the arm in the starting position. Four auditory cues guided subjects through the task [Color figure can be viewed at wileyonlinelibrary.com]

anti-aliasing filter with a half-power cutoff at 3.6 kHz was applied (see www.biosemi.com). The data were sampled at 512 Hz (2,048 Hz with a decimation factor of 1/4) with a bandwidth of 134 Hz, using a fifth order digital sync filter. Each active electrode was measured online with respect to a common mode sense active electrode producing a monopolar (non-differential) channel. Two additional electrodes were positioned on the external canthi (the bone at the side of the eye) for electrooculogram (EOG) recording. EEG data were down sampled to 256 Hz and then imported it into EEGLAB software (Delorme & Makeig, 2004) for further analysis and raw EEG between 0.1 and 100 Hz. Using visual inspection, we identified and removed segments of recording affected by artifacts due to subjects' movement. In particular, the percentage of removed events was $9.4 \pm 5.6\%$ for the P condition and $7.7 \pm 3.7\%$ for the VP condition (mean \pm SD), corresponding to 163.3 ± 10.2 and 165.9 ± 6.8 (mean \pm SD) trials performed in the P and VP condition, respectively.

We based visual identification of artifact on the topographical and spectral distribution, as well as on the time series of the independent component calculated with the ICA algorithm that EEGLAB implemented. We re-referenced data to the common average reference and we then extracted epochs from -600 to $1,000$ ms with respect to event (time = 0).

2.5 | Evaluating ERSP

For each epoch, we applied fast Fourier transform to partially overlapping time segments: each segment was 256 ms long (64 samples) and each shifting step was 8 ms. We also employed a 16 points zero-padding and a Hanning-window tapering to increase smoothness in ERSP estimation and to limit edge effects. To get a clean estimation of baseline spectral activity, we considered the period between $-1,100$ and -600 ms with respect to the initiation of the trial.

We calculated ERSPs as event-related power variations (in dB) compared to the specified baseline (Makeig, 1993), then averaged them across epochs for each condition considering times from 400 ms before to 400 ms after the event (8 ms resolution), and frequencies from 4 to 32 Hz (~ 0.5 Hz resolution).

2.6 | EEG data analysis

This study analyzed cortical activity in four regions of interest (ROIs). Precisely, we observed the activation of channels C3 and C4, which are considered to correspond to the hand motor area (Burle, Roger, Allain, Vidal, & Hasbroucq, 2008; Pfurtscheller, Neuper, Andrew, & Edlinger, 1997) (left hemisphere/right hand and right hemisphere/left hand, respectively) and channels CP1, CP3 and CP2, CP4 to collect information on the *sensorimotor area* (of left and right hemisphere) (Christensen et al., 2007). Furthermore, we considered two channels mostly representative of the *association area* (Herwig, Satrapi, & Schönfeldt-Lecuona, 2003): P1 for the left and P2 for the right hemisphere, and finally channels O1 and O2 identified the left and right *visual areas*, respectively (Neuper, Scherer, Reiner, & Pfurtscheller, 2005).

The four ROIs with their corresponding channels are summarized in Table 1 and are illustrated in Figure 2.

We analyzed data at the *onset* and the *offset* of the active matching movement, triggered at 2 cm/s velocity threshold. Precisely, the hand speed exceeding the 2 cm/s threshold marked the initiation or *onset* of the matching movement. Similarly, the hand crossing the 2 cm/s threshold for at least 2 s helped us detect the termination or *offset*. We considered the EEG during active movement *onset* and *offset* in four time windows: W1: -400 to -200 ms; W2: -200 to 0 ms; W3: 0 to 200 ms; and W4: 200 to 400 ms (see Figure 3).

Finally, based on previous literature, we evaluated the effects in the μ frequency band, which is traditionally defined as an 8–12 Hz rhythm that decreases, or desynchronizes, with movement (McFarland et al., 2000; Niedermeyer, 1997; Pfurtscheller & Aranibar, 1979).

2.7 | Behavioral data analysis

Hand position during the active movement was measured from the 17-bit encoders of the motor with a precision higher than 0.1 mm in the whole workspace. Hand speed (and subsequent derivatives) was estimated by using a fourth order Savitzky–Golay smoothing filter (with an equivalent cut off frequency of 6 Hz). As subjects' goal was to replicate, as accurate and precise as possible, the target position, we used two indicators that could best describe the overall subject

TABLE 1 In the left column, the ROIs names and the relative cortical areas whose activity is considered to be mostly reflected by the signals recorded from channels in the corresponding right column

ROIs (cortical areas)	Channels
Left/right hand motor area	C3/C4
Left/right somatosensory area	[CP1 CP3]/[CP2 CP4]
Left/right association area	P1/P2
Left/right visual area	O1/O2

We separately considered left and right hemispheres for a total of eight ROIs.

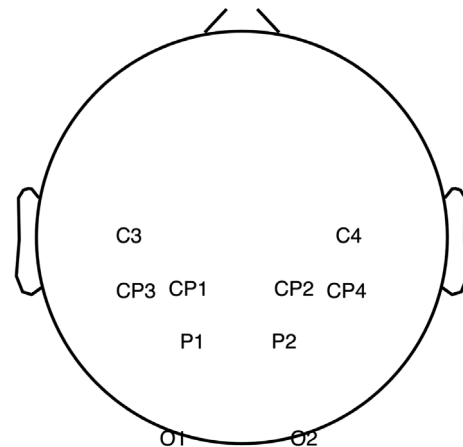


FIGURE 2 Channels corresponding to the considered regions of interest (ROIs)

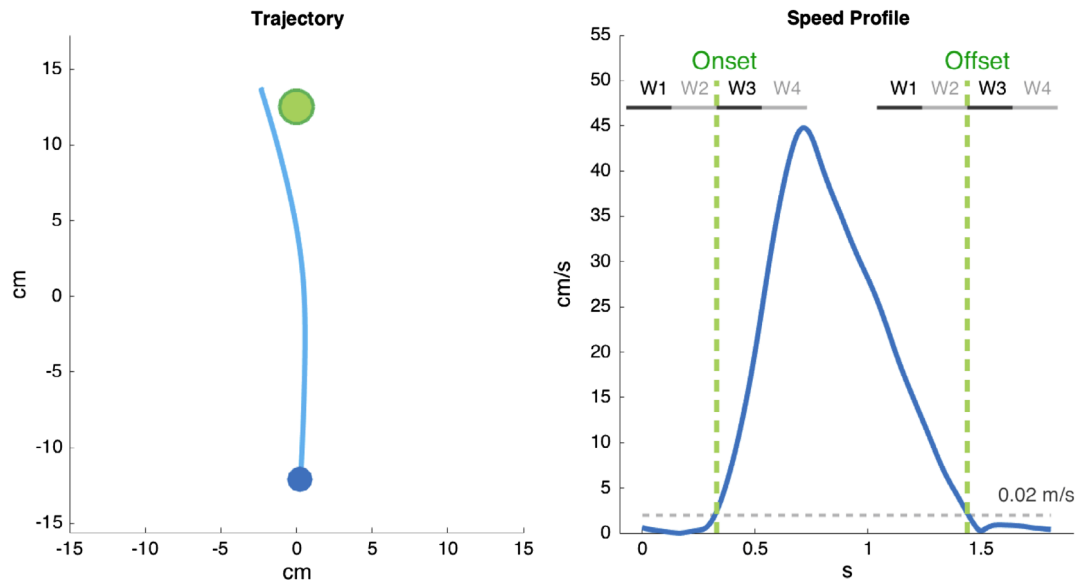


FIGURE 3 Sample trajectory (left panel) and the corresponding bell-shaped speed profile (right panel). Green dotted lines highlight movement onset and offset and the four time windows in which EEG signals have been averaged and analyzed [Color figure can be viewed at wileyonlinelibrary.com]

performance during each trial: the *Matching error*, *ME* and the *Variability*, *V*. The *Matching error* measures the accuracy of performance and it is computed as the averaged absolute deviation between the proprioceptive target position and the wrist configuration at the end of the active movement (Marini, Squeri, Morasso, Konczak, & Masia, 2016; Marini, Squeri, Morasso, & Masia, 2016).

$$ME = \frac{\sum_N \sqrt{(x_i - x_{TG})^2 + (y_i - y_{TG})^2}}{N} \quad (1)$$

where x_i and y_i are the x and y coordinates of the hand's final position at the end of the active matching movement in the i -trial, and x_{TG} and y_{TG} are the x and y coordinates of the ideal target position, both averaged across the N (120) target repetitions in each condition.

The *Variability* is evaluated, for each condition, as the *SD* across the N (120) trials, of hand's position at the end of the active movement and it provides information about subjects' performance consistency (or precision) (Marini, Squeri, Morasso, & Masia, 2016):

$$V = \sqrt{SD(x_{i=1:N})^2 + SD(y_{i=1:N})^2}. \quad (3)$$

2.8 | Statistical analysis

We divided the analysis of the EEG data in two parts. In the first part, for each ROI independently considered, ERSP underwent to an analysis of variance, considering the hemisphere and condition (VP and P) as factors. In the second part, we computed the difference between the ERSP in the VP and P condition (Δ_{VP-P}), then we performed an

analysis of variance (ANOVA) with consideration for the ROIs and hemispheres as factors. Significant effects were investigated with post hoc comparisons made by paired two-tailed t tests. Comparisons were considered significant when $p < 0.05$ after Bonferroni correction for multiple comparisons.

To investigate the nature of the differences between the P and VP condition of the *Matching error* and the *Variability*, we performed two independent paired two-tailed t tests and we considered the differences significant when $p < 0.05$.

3 | RESULTS

3.1 | Behavioral results

As expected, lower values of both *Matching error* and *Variability* were overall achieved in the VP condition (Figure 4). In particular the *ME* increased from 0.99 ± 0.23 cm (mean and SEM) in the VP condition to 2.41 ± 0.23 cm in the P condition ($t[22] = 11.96$, $p < 0.001$). Similarly, the *V* increased from 2.64 ± 0.35 cm in the VP condition to 4.17 ± 0.31 cm in the P condition ($t[22] = 5.40$, $p < 0.001$).

3.2 | Differences in hemispheres, between the VP and P condition

Figure 5 shows desynchronization in the μ band, during W2, that is, in the 200 ms interval preceding movement's *onset* and *offset*. The P condition (top panels) presents substantial activation in the hand motor and somatosensory areas, with low involvement of other areas. Besides, such activation affects almost the entire left hemisphere.

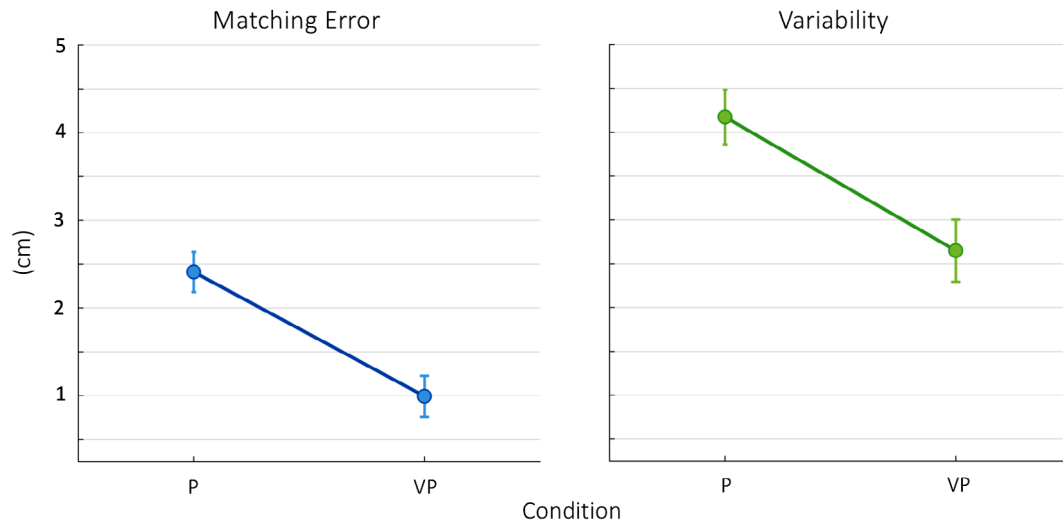


FIGURE 4 Mean and SE of matching error (left panel) and variability (right panel) in visuoproprioceptive (VP) and proprioceptive (P) conditions [Color figure can be viewed at wileyonlinelibrary.com]

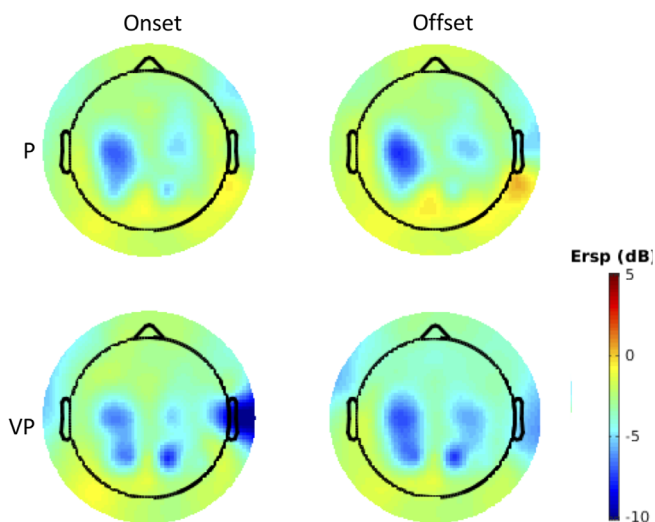


FIGURE 5 Desynchronization pattern in the μ band in the 200 ms preceding the event. Top and bottom lines show desynchronization in the two events (onset, offset) in the visuoproprioceptive (VP) and proprioceptive (P) conditions [Color figure can be viewed at wileyonlinelibrary.com]

The VP condition (bottom panels) shows desynchronization in the hand motor and somatosensory areas, which is not only higher in the left hemisphere, but also involves the right hemisphere; moreover, the visual and association areas show specific bilateral desynchronization.

The following paragraphs report the difference in the ERSPs under VP and P conditions in the two hemispheres of the four brain areas. Moreover, results are presented for the four time windows (W1–W4) related to movement *onset* and *offset*.

3.3 | Activity in the somatosensory areas

Figure 6a shows the ERSP curve in the somatosensory area during movement's *onset* (left panel) and *offset* (right panel). At movement

onset, a higher desynchronization was found in the left hemisphere. A higher desynchronization appeared in the VP condition for both hemispheres. At movement's *offset*, the higher desynchronization in the left hemisphere persisted, while we mainly identified dissimilarities between conditions after the *offset* event.

At the *onset* of the active matching movement, ANOVA reported a main effect of hemisphere in the four time windows due to substantially higher desynchronization in the left hemisphere both a movement *onset*, top panels of Figure 6b, (W1: $F_{1,22} = 28.32$, $p < 0.001$; W2: $F_{1,22} = 35.44$, $p < 0.001$; W3: $F_{1,22} = 29.86$, $p < 0.001$; W4: $F_{1,22} = 21.69$, $p < 0.001$) and *offset*, Figure 5b bottom panels, (W1: $F_{1,22} = 15.30$, $p < 0.001$; W2: $F_{1,22} = 14.63$, $p < 0.001$; W3: $F_{1,22} = 20.82$, $p < 0.001$; W4: $F_{1,22} = 19.59$, $p < 0.001$).

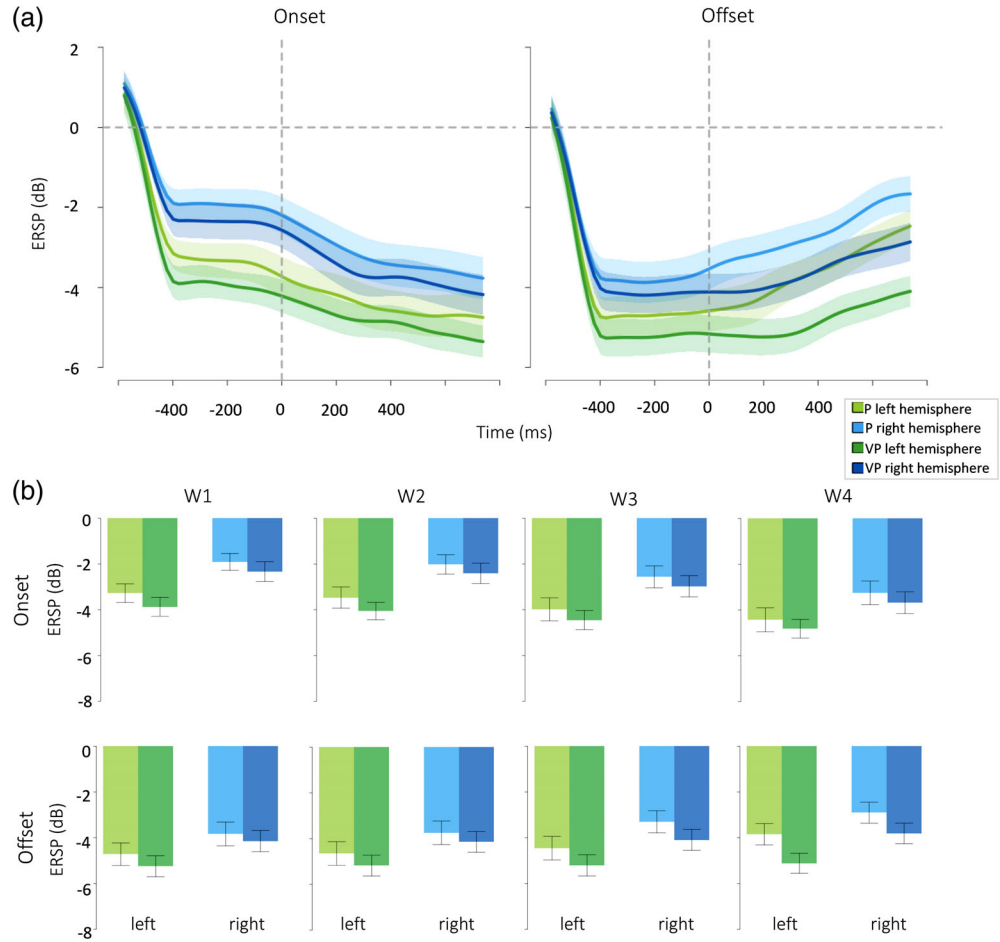
As well, a main effect of the condition emerged before movement *onset*, Figure 6b top panels, (W1: $F_{1,22} = 6.09$, $p = 0.021$; W2: $F_{1,22} = 6.34$, $p = 0.019$) and persisted after the event, Figure 6b's bottom panels (W3: $F_{1,22} = 7.84$, $p = 0.014$; W4: $F_{1,22} = 4.95$, $p = 0.036$). The main effect of condition became significant at movement's *offset* only after the event (W3: $F_{1,22} = 6.88$, $p = 0.015$; W4: $F_{1,22} = 13.93$, $p = 0.001$), which the bottom panels of Figure 6b clearly show. In all cases, when the two conditions diverged, the VP presented the highest desynchronization.

3.4 | Activity in the hand motor areas

Figure 7a shows the ERSP curves in the hand motor area during movement's *onset* (left panel) and *offset* (right panel). In both phases, there appeared a clear higher desynchronization of the left hemisphere. Furthermore, while at movement's *onset* no differences emerged between the two conditions; in the left hemisphere, condition substantially affected the desynchronization at movement's *offset*, with a higher desynchronization in case of VP condition.

At the *onset* of the active matching movement, ANOVA reported the main effect of hemisphere in the four time windows (W1:

FIGURE 6 (a) Event-related spectral perturbation (ERSP) curves in the somatosensory area during movement's onset (left panel) and offset (right panel). Green and blue lines represent the desynchronization in the left and right hemispheres, respectively. Dark green and dark blue indicate the visuo-proprioceptive condition; the proprioceptive condition is represented in light green and light blue. (b) ERSP values in the four considered time windows for the left and right hemisphere in the two conditions [Color figure can be viewed at wileyonlinelibrary.com]



$F_{1,22} = 14.02$, $p = 0.001$; W2: $F_{1,22} = 15.05$, $p < 0.001$; W3: $F_{1,22} = 16.64$, $p < 0.001$; W4: $F_{1,22} = 14.02$, $p = 0.001$) due to a substantially higher desynchronization in the left hemisphere (Figure 7b, top panels). In addition, at the *offset* of the matching movement, we found a main effect of hemisphere in the four time windows (W1: $F_{1,22} = 18.14$, $p < 0.001$; W2: $F_{1,22} = 19.84$, $p < 0.001$; W3: $F_{1,22} = 22.78$, $p < 0.001$; W4: $F_{1,22} = 22.89$, $p < 0.001$) due to a substantially higher desynchronization in the left hemisphere (Figure 7b, bottom panels).

We determined a significant interaction between hemisphere and condition in the four time windows (W1: $F_{1,22} = 12.93$, $p < 0.001$; W2: $F_{1,22} = 16.40$, $p < 0.001$; W3: $F_{1,22} = 11.36$, $p = 0.002$; W4: $F_{1,22} = 9.49$, $p = 0.005$).

The post hoc test then highlighted that the μ band desynchronization in the VP condition was stronger than in the P condition, though only in the left hemisphere. This pattern was continuously maintained from the time window just before the movement's *offset* W2 (left: $t(22) = 2.55$, $p = 0.003$, right: $t(22) = -1.06$, $p = 0.6$), to the time windows after the event W3 (left: $t(22) = 2.65$, $p = 0.029$, right: $t(22) = -0.25$, $p = 1$) and W4 (left: $t(22) = 2.95$, $p = 0.014$, right: $t(22) = 0.37$, $p = 1$). However, it was identifiable also in the early stage at W1, even though only in the form of a trend since the difference did not reach significance (left: $t(22) = 2.38$, $p = 0.052$, right: $t(22) = -1.47$, $p = 0.3$).

3.5 | Activity in the association areas

Figure 8a shows the ERSP curve in the association areas during movement's *onset* (left panel) and *offset* (right panel). For both the events and hemispheres, a higher desynchronization appeared in the VP condition. The higher desynchronization was more pronounced at movement's *offset*.

At the onset of the active matching movement, ANOVA reported a main effect of condition which started with a trend in the early time window (W1: $F_{1,22} = 3.89$, $p = 0.061$), then became fully significant (W2: $F_{1,22} = 5.54$, $p = 0.029$; W3: $F_{1,22} = 7.19$, $p = 0.013$; W4: $F_{1,22} = 5.96$, $p = 0.023$). Specifically, top panels of Figure 8b show how, at movement *onset*, desynchronization is stronger in the VP than in the P condition.

Movement's *offset* showed a similar but more pronounced pattern (Figure 8b, bottom panels) in all time windows (W1: $F_{1,22} = 9.66$, $p = 0.005$; W2: $F_{1,22} = 11.85$, $p = 0.002$; W3: $F_{1,22} = 16.61$, $p < 0.001$ and W4: $F_{1,22} = 16.68$, $p < 0.001$).

3.6 | Activity in the visual areas

Figure 9b shows the ERSP curve in the visual areas during movement's *onset* (left panel) and *offset* (right panel). While at movement's *onset* the condition did not modulate the desynchronization, at

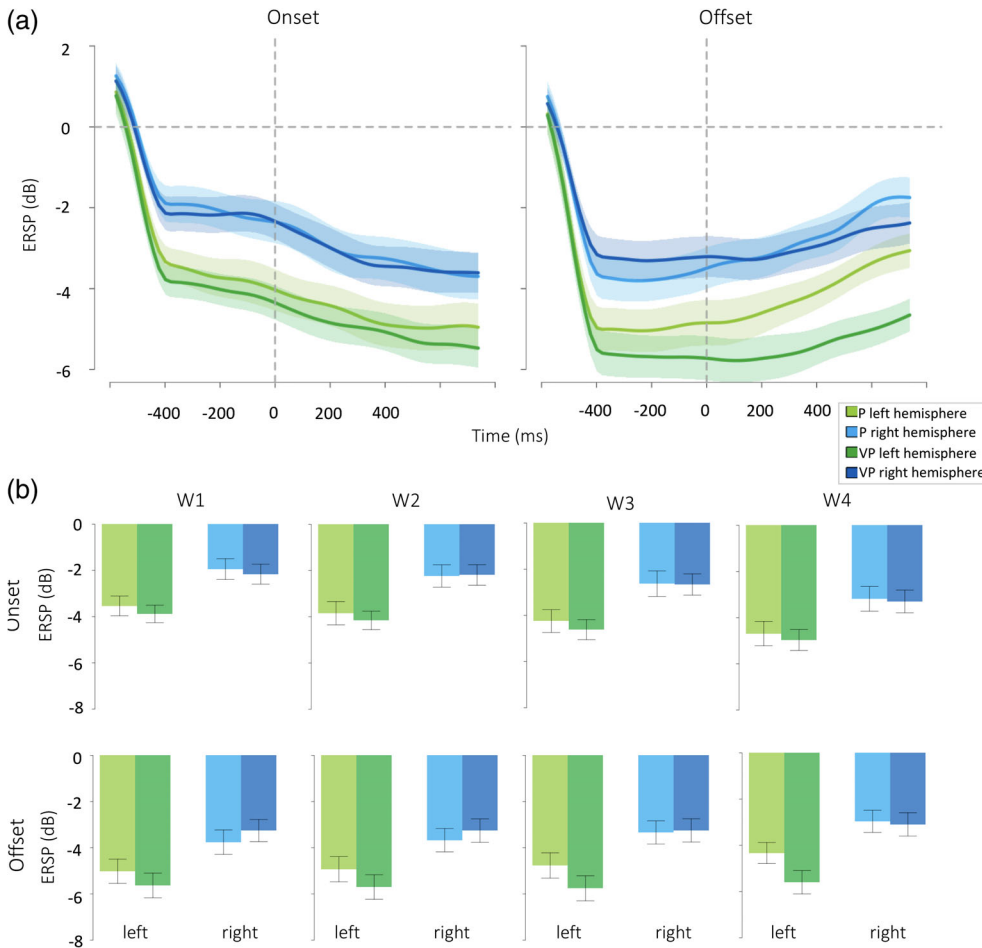


FIGURE 7 (a) Event-related spectral perturbation (ERSP) curves in the hand motor area during movement's onset (left panel) and offset (right panel). Green and blue lines represent the desynchronization in the left and right hemispheres, respectively. Dark green and dark blue indicate the visuo-proprioceptive condition; the proprioceptive condition is represented in light green and light blue. (b) ERSP values in the four considered time windows for the left and right hemisphere in the two conditions [Color figure can be viewed at wileyonlinelibrary.com]

movement's *offset* the VP condition presented a dramatic higher desynchronization.

At movement's *offset*, the desynchronization in the visual area was consistently higher (Figure 9b bottom panel). The effect began in the W1 time window ($F_{1,22} = 13.6940$, $p = 0.0012$) and remained strong in the W2 ($F_{1,22} = 30.1237$, $p < 0.001$), W3 ($F_{1,22} = 36.5622$, $p < 0.001$), and W4 ($F_{1,22} = 35,8,199$, $p < 0.0001$) time windows.

3.7 | Influence of the ROI on the difference between VP and P conditions

Having discussed the different activities and their areas, the second aim of the current study is to unveil how the ROI (motor, somatosensory, association, and visual areas) and the hemisphere modulated the value of the ERSP difference between the VP and P condition (Δ_{VP-P}).

Figure 10 shows the Δ_{VP-P} in the two hemispheres for all four ROIs. We separately considered *onset* (top panels) and *offset* (bottom panels) movement's phases. At movement's *onset*, neither the hemisphere nor the ROI showed any modulation on the Δ_{VP-P} . Instead, at movement's *offset*, the ROI modulated the difference between the two conditions (W1: $F_{3,66} = 8.48$, $p < 0.001$; W2: $F_{3,66} = 10.58$, $p < 0.001$; W3: $F_{3,66} = 13.48$, $p < 0.001$; W4: $F_{3,66} = 9.48$, $p < 0.001$) and the hemispheres (W1: $F_{1,22} = 5.70$, $p = 0.026$; W2: $F_{1,22} = 7.40$, $p = 0.012$; W3: $F_{1,22} = 8.63$, $p < 0.001$; W4: $F_{1,22} = 12.91$, $p = 0.001$).

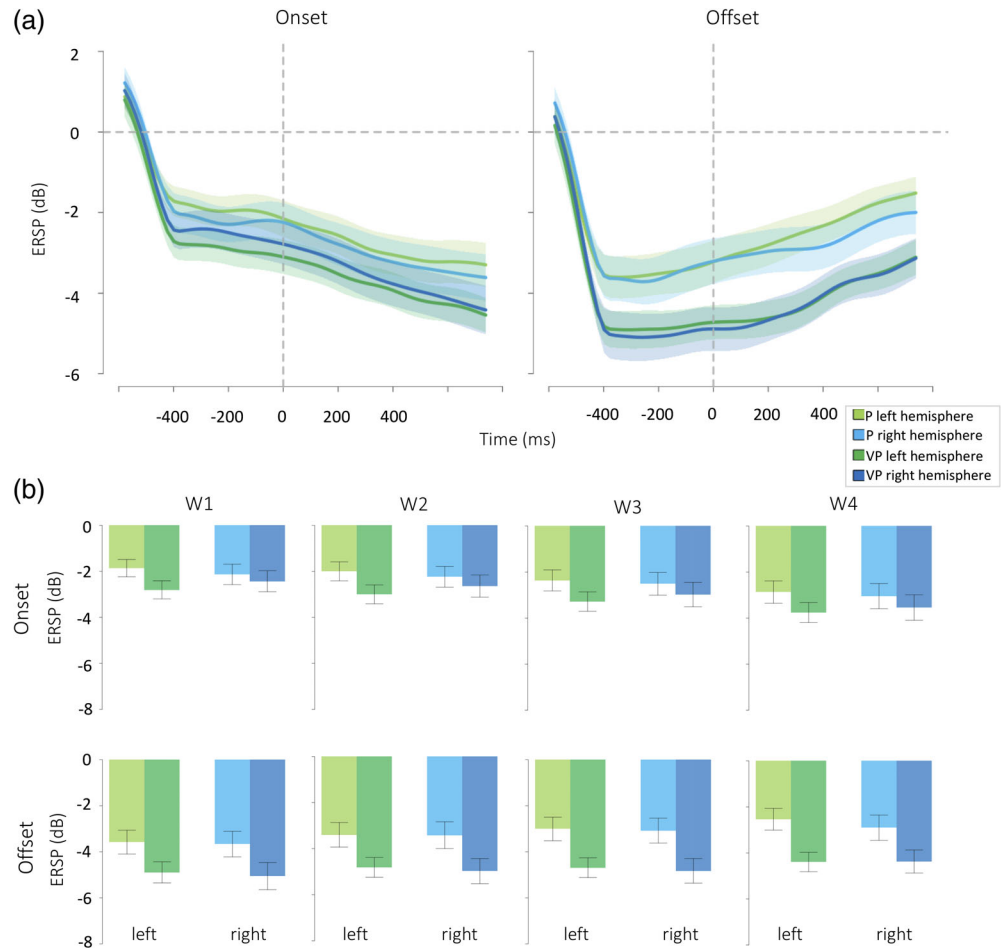
As well, we identified significant interaction between ROI and hemisphere in the four time windows (W1: $F = 5.46$, $p = 0.002$; W2: $F = 10.58$, $p < 0.001$; W3: $F = 13.48$, $p < 0.001$, and W4: $F = 9.48$, $p < 0.001$).

Figure 10's bottom panels highlight how, in the left hemisphere, and in all four time windows Δ_{VP-P} was smaller in the sensory area, increased in the motor area, and reached the highest value in the association and visual areas.

Post hoc analysis revealed that Δ_{VP-P} was stronger in the sensory area than in the motor area until 200 ms after the event (W1: $t(22) = 3.06$, $p = 0.005$; W2: $t(22) = 3.82$, $p = 0.011$; W3: $t(22) = 4.05$, $p = 0.006$). From the first 200 ms before the event, Δ_{VP-P} was stronger in the visual area than both in the motor (W2: $t(22) = 4.17$, $p = 0.004$; W3: $t(22) = 4.63$, $p = 0.001$; W4: $t(22) = 3.93$, $p = 0.009$) and sensory area (W2: $t(22) = 3.87$, $p = 0.009$; W3: $t(22) = 4.69$, $p = 0.001$; W4: $t(22) = 4.31$, $p = 0.003$).

We found no similar pattern in the right hemisphere for Δ_{VP-P} ; moreover, differences were not only less significant, but also only the comparison between the motor area versus the association (W1: $t(22) = 3.61$, $p = 0.018$; W2: $t(22) = 3.48$, $p = 0.025$; W3: $t(22) = 3.21$, $p = 0.048$) and visual area (W1: $t(22) = 3.93$, $p = 0.008$; W2: $t(22) = 3.55$, $p = 0.023$; W3: $t(22) = 3.080$, $p = 0.011$; W4: $t(22) = 3.55$, $p = 0.019$) resulted significant. A difference emerged between Δ_{VP-P}

FIGURE 8 (a) Event-related spectral perturbation (ERSP) curves in the association area during movement's onset (left panel) and offset (right panel). Green and blue lines represent the desynchronization in the left and right hemispheres, respectively. Dark green and dark blue indicate the visuo-proprioceptive condition; the proprioceptive condition is represented in light green and light blue. (b) ERSP values in the four considered time windows for the left and right hemisphere in the two conditions [Color figure can be viewed at wileyonlinelibrary.com]



in the association area versus the motor area in the early time window (W1: $t(22) = -3.45$, $p = 0.029$).

4 | DISCUSSION

Human beings are superbly moving animals. Proprioception allows us to sense body movements or positioning, which is essential for precisely controlling motion. Proprioception is a peculiar sensory modality with features that separate it from the others like vision or audioception. First of all, it lacks a specific sense organ, like eyes or ears, but it is distributed across the body, with primary sensory cells in the skin, muscle spindles, joints, and tendons (Gandevia & McCloskey, 1976; Gandevia, Refshauge, & Collins, 2002). Moreover, the whole set of primary receptors is subdivided into many classes with very different sensing properties (Proske, 2006). Significant multisensory data fusion of proprioceptive signals is therefore necessary, both at the peripheral and central levels, before functionally relevant proprioceptive information is distilled and usable in unconscious or conscious sensorimotor mechanisms. The interplay of proprioceptive feedback, muscle properties, and feedforward control has been the subject of continuous investigation in relation to the termination of voluntary movements, such as in the case of the reaching movement of the arm (Bizzi, Polit, & Morasso, 1976).

The early hypothesis that proprioceptive feedback might terminate the pattern of supraspinal commands, which initiate voluntary movements, in a comparison with a target set point (Gibbs, 1954), came under scrutiny in the form of experimental evidence. The evidence indicates that chronic deafferentation, due either to rhizotomy in monkeys (Bizzi et al., 1976; Taub, Goldberg, & Taub, 1975), peripheral neuropathy, or cerebrovascular accidents in humans (Lashley, 2017; Volpe, LeDoux, & Gazzaniga, 1979), demonstrates that centrally initiated movements can be executed accurately even in the absence of sensory feedback. On the other hand, subsequent studies on the recovery of voluntary movement following transection of dorsal roots has clarified that preoperative "elegance" and smoothness of movements are never fully recovered (Bossom, 1974). Moreover, it is difficult for deafferented experimental animals or human patients lacking proprioceptive inputs to perform normal multijoint limb movements even though they can initiate limb movements (Ghez, Gordon, & Ghilardi, 1995; Sainburg, Ghilardi, Poizner, & Ghez, 1995). The study of some rare clinical cases of extensive neuropathy, massively and permanently depriving the brain of its primary sources of dynamogenic information from skin and muscles, highlights the key role of proprioceptive afferents for calibrating the spatial motor frame of reference (Bard, Fleury, Teasdale, Paillard, & Nougier, 1995), that is, a crucial problem of motor cognition, beyond the specific details of motor control. This

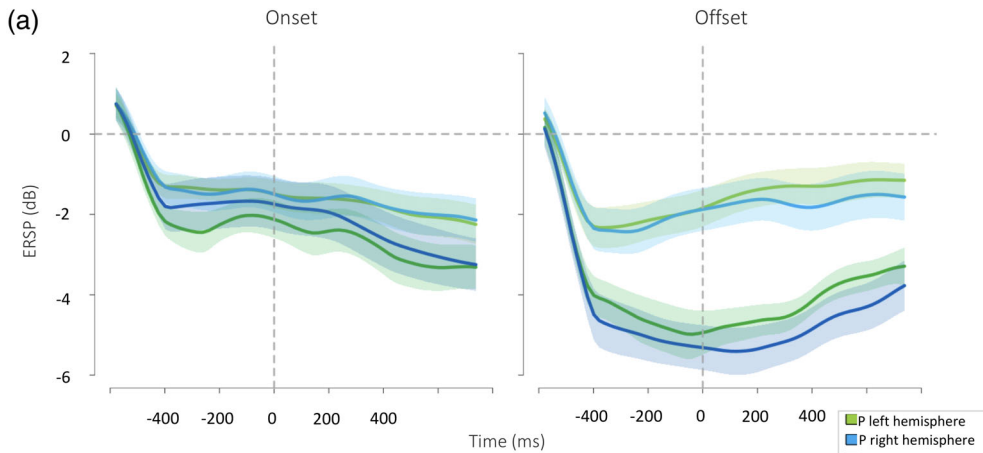


FIGURE 9 (a) Event-related spectral perturbation (ERSP) curves in the visual area during movement's onset (left panel) and offset (right panel). Green and blue lines represent the desynchronization in the left and right hemispheres, respectively. Dark green and dark blue indicate the visuo-proprioceptive condition; the proprioceptive condition is represented in light green and light blue. (b) ERSP values in the four considered time windows for the left and right hemisphere in the two conditions [Color figure can be viewed at wileyonlinelibrary.com]

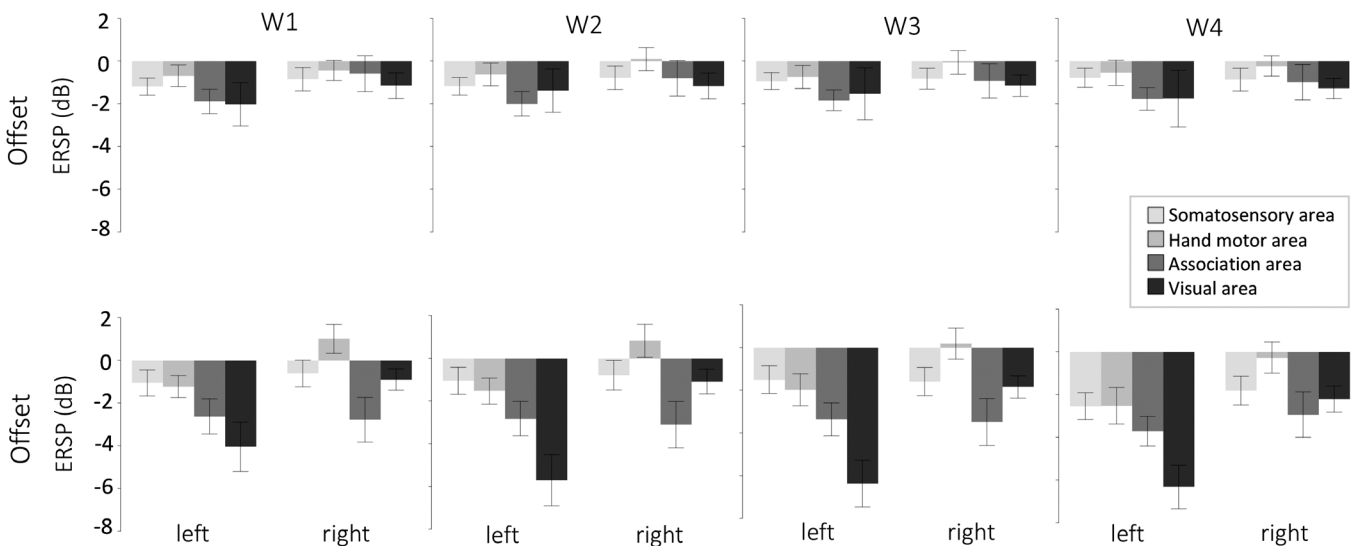
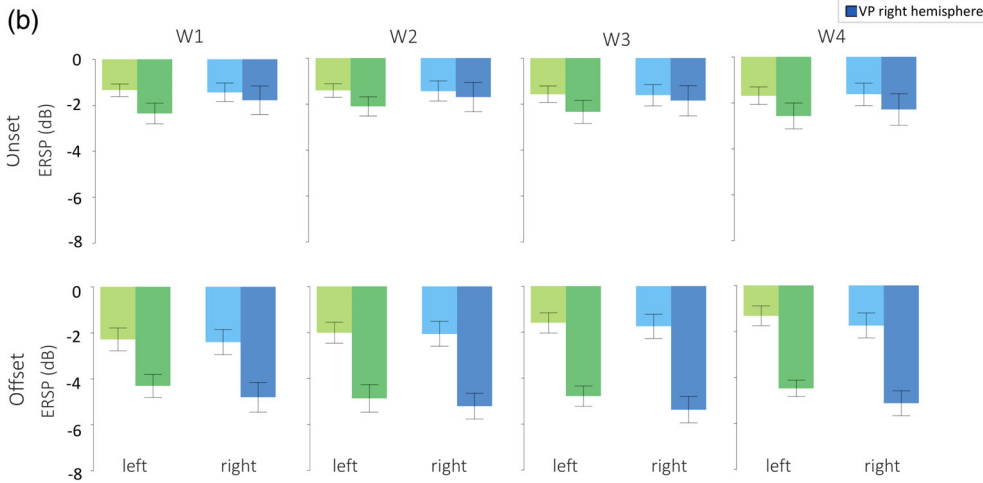


FIGURE 10 Difference between μ desynchronization in visuo-proprioceptive (VP) and proprioceptive (P) condition ($\Delta_{VP - P}$) in the three regions of interest (ROIs) for the left and right hemispheres, at movement's onset (top panels) and movement offset (bottom panels)

is also linked to the studies that address the effects of deafferentation on mental/motor imagery (Alkadhi et al., 2005; ter Horst, Cole, van Lier, & Steenbergen, 2012), which demonstrate significant impairment of motor imagery processes.

Such evidence indicates that sensory afferent inputs that convey kinesthetic or proprioceptive information to the brain are an important vehicle for the brain to archive precise and elaborate limb movement control. It may also be the case that the kinesthetic feedback

information during limb movements plays a crucial role when acquiring motor skills (Naito, 2004).

It thereby appears that in the hierarchy of sensorimotor processes, from reflex mechanisms to motor cognitive processes, the role of proprioception may become increasingly strong. This is especially true considering the importance of the internal body model for integrating the same framework of overt and covert purposive actions and the fact that proprioception might act as a mediator that keeps together the different parts of the model (Mohan, Bhat, & Morasso, 2018).

Despite the impact that proprioceptive deficits have in everyday life activities, such as posture and gait control, little is yet known about the neural correlates of upper limb positioning senses. To fill this gap, we investigated the reduction of the desynchronization in the μ frequency band during an active, upper limb, position-matching task that the robotic device performed.

4.1 | Lateralization of activation in the different ROIs

As a primary result, we observed higher activation in the left motor and somatosensory areas, contralateral to the moving limb. There are two aspects to this finding: first, the strongest desynchronization was reached in those areas which normally participate in executing movements of the corresponding limb (Naito et al., 2005); second, the hemisphere lateralization of proprioceptive-related brain activation emerged exclusively in motor and somatosensory areas—this is supported by current knowledge of contralateral dominance in limb movement perception (Naito et al., 2007). Vice versa, both the parietal and occipital regions of the two hemispheres, which identify association and visual areas, respectively, exhibited similar activation levels.

Furthermore, current literature has extensively demonstrated that an activation in ipsilateral motor cortex accompanies hand movements (Cramer, Finklestein, Schaechter, Bush, & Rosen, 1999). Our study confirms and extends these findings, and thereby suggests that processing position sense could also be effectively located in the contralateral hemisphere.

This concept well fits with previous evidences of hemispheric lateralization of somatosensory processing (Coghill & Iadarola, 2001) extending early findings of deficits in contralateral tactile sensibility resulting from unilateral lesions to either the primary or secondary somatosensory cortex (Greenspan & Winfield, 1992; Marshall, 1951). Similarly, it was also demonstrated that direct electrical stimulation of those areas produces sensations that are generally referred to a contralateral portion of the body (Becker, 1953). Despite the capacity of each cerebral cortical hemisphere to subserve components of somatosensory processing, substantial evidence indicates that both hemispheres can be engaged in the processing of a unilateral somatosensory stimulus via bilateral subcortical routes. Accordingly, the light activation we found in the right (ipsilateral) hemisphere can be explained by previous theories showing that the right posterior parietal cortex is critical for attentional aspects of somatosensory processing, since lesions of this structure result in a unilateral neglect in which subjects have diminished awareness of tactile stimuli applied to left portions of the body (Mesulam, 1981). More specifically related

to proprioception and kinesthesia, the present data show a dominance of the contralateral (i.e., left) hemisphere in brain activation during proprioceptive tasks and they need to be further explored in light to other fMRI findings showing right-sided areas significantly more activated than the corresponding areas in the left hemisphere in human kinesthetic processing (Naito et al., 2005). However, it is worth considering that our results go in parallel with these mentioned fMRI studies as in this last case subjects experience illusory limb movements elicited by tendon vibration but not actual movements. Furthermore, a possible explanation for this discrepancy between our results and these imaging experiments (Naito et al., 2005) suggesting the right hemisphere is more important for proprioception, may lie in the adopted methodology: current experimental designs cannot isolate the proprioceptive sense through direct manipulations that help one sense one's body in an experimental condition but not in another and both the conditions designed involve a high motor component.

4.2 | Differences in the brain activation between VP and P condition

The neural correlates of proprioception investigated in this study allowed us to identify the natural synergy between proprioception and vision. Although dozens of neurophysiological studies, especially in monkeys, have examined the role of vision in the control of movement (Graziano & Gross, 1998; Rizzolatti, Luppino, & Matelli, 1998), as of 2019 little is known about how these signals combine in the brain.

Generally, we found stronger activation levels in the μ band in the condition with visual feedback.

When the visual feedback of hand's position was provided, such high desynchronization possibly relies on the interactions between different sensory modalities (i.e., proprioception and vision) and may contribute to better understanding body-related sensory processing (Tsakiris, Hesse, Boy, Haggard, & Fink, 2007).

4.3 | Modulation of the difference between VP and P condition by the ROI

In this current study, we also determined that the four brain areas modulated the difference in the μ desynchronization under the two feedback conditions differently, with less influence in motor and somatosensory areas. This suggests the proprioceptive processing of arm position and movement is done by the motor and somatosensory areas no matter whether the visual feedback is also provided and consolidate proprioception as an equally important sensory modality as vision.

Previous hypotheses support this interpretation, suggesting that kinesthetic processing of the muscle spindle afferent inputs takes place in the multiple motor areas that normally participate in generating voluntary limb movement (Naito, 2004). This means that identical sections of multiple motor areas engage in kinesthetic sensory processing and in generating corresponding limb movement (Ciccarelli et al., 2005; Weiller et al., 1996). It is therefore possible that neuronal

populations in these areas that generate motor activity also process kinesthetic signals related to the same movement. This functional organization could efficiently facilitate sensorimotor integration in human motor control.

On the contrary, occipital and parietal areas are accountable for visual processing and integration of different sensory information (Rizzolatti et al., 1998), respectively, and they are widely influenced by the modality and the number of the sensory feedback conditions. Recent experiments also indicate that sensory signals from many modalities, as well as efference copy signals from motor structures, converge in the posterior parietal cortex to code the spatial locations of goals for movement (Andersen, Snyder, Bradley, & Xing, 1997). One might therefore logically assume that the activation in the region is proportional to the number of sensory signals converging.

Furthermore, despite only few investigations into brain regions responsible for position sense in humans exist, recent studies identified that a distributed network of brain areas appear to be responsible for processing position sense (Findlater et al., 2016, 2018). These studies, involving two complimentary lesion analyses [statistical region of interest and voxel-based lesion-symptom mapping (Bates et al., 2003)] and testing stroke subjects, helped to refine the understanding of human brain areas involved in processing the conscious appreciation of position sense and particularly identified the parietal lobe structures (postcentral, superior parietal, inferior parietal, angular, and supramarginal gyri) as essential for intact position sense.

In case of acute stroke survivors, it was shown that damage to the postcentral gyrus and posterior parietal cortex was associated with poor position sense (Findlater et al., 2016) and that also damage to the arcuate fasciculus, inferior frontal gyrus, superior temporal gyrus, postcentral gyrus, insula and Rolandic operculum was also associated with decreased proprioception, thus suggesting that a relatively distributed network is responsible for processing position sense which is interesting and crucial for the interpretation of our results.

4.4 | The difference in the neural correlates between P and VP condition emerged at movement's offset

Regarding the difference in the neural correlates between proprioception and VP conditions that emerged in this study, such emergence mostly affected the desynchronization at movement's offset with low or no influence at the onset of movement.

We have reasons to deduce the logic of this study's results from the experimental protocol itself: the instruction given to the subject was "replicate the target position as accurate as possible" and so most of the proprioceptive processing and sensory information centrally collected were recalled in proximity to the final position, when the finest motor control output had to be executed. These results offer reason to believe that the feedback condition affected the motor planning, not before movement onset, but when the process of preparing the appropriate motor commands is mostly needed for successful task execution (Orban de Xivry, Legrain, & Lefèvre, 2017).

4.5 | Limitations and future perspectives

Even though using a robotic device allowed this study to guarantee repeatability and consistency in the proprioceptive test, the limitations of the spatial and temporal resolution of the EEG measurement techniques did not permit precise associations between brain activation and specific action parameters, as well as the regions involved. It is necessary for future studies to fully elucidate these elements.

Furthermore, the two experimental conditions are unbalanced, since one involves visual and proprioceptive feedbacks while the other involves only proprioceptive feedback. This is because classical experimental designs cannot isolate the sense of body ownership through direct manipulations that help one sense one's body in an experimental condition but not in another (Tsakiris et al., 2007). This results in difficulty experimentally studying the neural and functional signatures of proprioception.

5 | CONCLUSIONS

In summary, our current study identified a lateralization of activation in motor and somatosensory areas and no lateralization in visual and association areas. We also saw that the condition with visual feedback entailed a stronger activation in the μ band with difference between condition being modulated by the ROI and less affecting motor and somatosensory area. Our final results showed that the difference in the neural correlates between P and VP conditions only emerged at movement's offset.

DATA AVAILABILITY STATEMENT

Raw data were generated at the Motor Learning, Assistive and Rehabilitation Robotics Laboratory of the Istituto Italiano di Tecnologia. Derived data supporting the findings of this study are available from the corresponding author FM on request.

ORCID

Francesca Marini  <https://orcid.org/0000-0003-4153-8053>

REFERENCES

- Alary, F., Doyon, B., Loubinoux, I., Carel, C., Boulanouar, K., Ranjeva, J. P., ... Chollet, F. (1998). Event-related potentials elicited by passive movements in humans: Characterization, source analysis, and comparison to fMRI. *NeuroImage*, 8(4), 377–390.
- Alegre, M., Labarga, A., Gurtubay, I. G., Iriarte, J., Malanda, A., & Artieda, J. (2002). Beta electroencephalograph changes during passive movements: Sensory afferences contribute to beta event-related desynchronization in humans. *Neuroscience Letters*, 331(1), 29–32.
- Alkadhi, H., Brugger, P., Boendermaker, S. H., Crelier, G., Curt, A., Hepp-Reymond, M.-C., & Kollias, S. S. (2005). What disconnection tells about motor imagery: Evidence from paraplegic patients. *Cerebral Cortex*, 15(2), 131–140.

- Andersen, R. A., Snyder, L. H., Bradley, D. C., & Xing, J. (1997). Multimodal representation of space in the posterior parietal cortex and its use in planning movements. *Annual Review of Neuroscience*, *20*(1), 303–330.
- Bard, C., Fleury, M., Teasdale, N., Paillard, J., & Nougier, V. (1995). Contribution of proprioception for calibrating and updating the motor space. *Canadian Journal of Physiology and Pharmacology*, *73*(2), 246–254.
- Bastian, H. C. (1887). On different kinds of aphasia, with special reference to their classification and ultimate pathology. *BMJ*, *2*(1401), 985–990.
- Bates, E., Wilson, S. M., Saygin, A. P., Dick, F., Sereno, M. I., Knight, R. T., & Dronkers, N. F. (2003). Voxel-based lesion-symptom mapping. *Nature Neuroscience*, *6*(5), 448–450.
- Becker, R. F. (1953). The cerebral cortex of man. By Wilder Penfield and Theodore Rasmussen. The Macmillan company, New York, N.Y. 1950. 248 pp. *American Journal of Physical Anthropology*, *11*(3), 441–444.
- Bernier, P. M., Burle, B., Hasbroucq, T., & Blouin, J. (2009). Spatio-temporal dynamics of reach-related neural activity for visual and somatosensory targets. *NeuroImage*, *47*(4), 1767–1777.
- Bizzi, E., Polit, A., & Morasso, P. (1976). Mechanisms underlying achievement of final head position. *Journal of Neurophysiology*, *39*(2), 435–444.
- Bossom, J. (1974). Movement without proprioception. *Brain Research*, *71* (2–3), 285–296.
- Burle, B., Roger, C., Allain, S., Vidal, F., & Hasbroucq, T. (2008). Error negativity does not reflect conflict: A reappraisal of conflict monitoring and anterior cingulate cortex activity. *Journal of Cognitive Neuroscience*, *20* (9), 1637–1655.
- Casadio, M., Sanguineti, V., Morasso, P. G., & Arrichiello, V. (2006). Braccio di Ferro: A new haptic workstation for neuromotor rehabilitation. *Technology and Health Care*, *14*(3), 123–142.
- Christensen, M. S., Lundbye-Jensen, J., Geertsen, S. S., Petersen, T. H., Paulson, O. B., & Nielsen, J. B. (2007). Premotor cortex modulates somatosensory cortex during voluntary movements without proprioceptive feedback. *Nature Neuroscience*, *10*(4), 417–419.
- Ciccarelli, O., Toosy, A. T., Marsden, J. F., Wheeler-Kingshott, C. M., Sahyoun, C., Matthews, P. M., ... Thompson, A. J. (2005). Identifying brain regions for integrative sensorimotor processing with ankle movements. *Experimental Brain Research*, *166*(1), 31–42.
- Coghill, R., & Iadarola, M. (2001). Hemispheric lateralization of somatosensory processing development of novel non-opioid therapies for pain control: Transcriptomic lead development to new drug application view project chronic pain after delivery view project. *Artic Journal of Neurophysiology*, *85*(6), 2602–2612.
- Cramer, S. C., Finklestein, S. P., Schaechter, J. D., Bush, G., & Rosen, B. R. (1999). Activation of distinct motor cortex regions during ipsilateral and contralateral finger movements. *Journal of Neurophysiology*, *81*(1), 383–387.
- Delorme, A., & Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods*, *134*(1), 9–21.
- Dukelow, S. P., Herter, T. M., Moore, K. D., Demers, M. J., Glasgow, J. I., Bagg, S. D., ... Scott, S. H. (2010). Quantitative assessment of limb position sense following stroke. *Neurorehabilitation and Neural Repair*, *24*(2), 178–187.
- Findlater, S. E., Desai, J. A., Semrau, J. A., Kenzie, J. M., Rorden, C., Herter, T. M., ... Dukelow, S. P. (2016). Central perception of position sense involves a distributed neural network – Evidence from lesion-behavior analyses. *Cortex*, *79*, 42–56.
- Findlater, S. E., Hawe, R. L., Semrau, J. A., Kenzie, J. M., Yu, A. Y., Scott, S. H., & Dukelow, S. P. (2018). Lesion locations associated with persistent proprioceptive impairment in the upper limbs after stroke. *NeuroImage Clinical*, *20*, 955–971.
- Gandevia, S. C., & McCloskey, D. I. (1976). Joint sense, muscle sense, and their combination as position sense, measured at the distal interphalangeal joint of the middle finger. *The Journal of Physiology*, *260*(2), 387–407.
- Gandevia, S. C., Refshauge, K. M., & Collins, D. F. (2002). Proprioception: Peripheral inputs and perceptual interactions. *Advances in Experimental Medicine and Biology*, *508*, 61–68.
- Ghez, C., Gordon, J., & Ghilardi, M. F. (1995). Impairments of reaching movements in patients without proprioception. II. Effects of visual information on accuracy. *Journal of Neurophysiology*, *73*(1), 361–372.
- Gibbs, C. B. (1954). The continuous regulation of skilled response by kinaesthetic feed back. *The British Journal of Psychology General Section*, *45*(1), 24–39.
- Goble, D. J. (2010). Proprioceptive acuity assessment via joint position matching: From basic science to general practice. *Physical Therapy*, *90*, 1176–1184.
- Goble, D. J., Coxon, J. P., Van Impe, A., Geurts, M., Doumas, M., Wenderoth, N., & Swinnen, S. P. (2011). Brain activity during ankle proprioceptive stimulation predicts balance performance in young and older adults. *The Journal of Neuroscience*, *31*, 16344–16352.
- Goble, D. J., Coxon, J. P., Van Impe, A., Geurts, M., Van Hecke, W., Sunaert, S., ... Swinnen, S. P. (2012). The neural basis of central proprioceptive processing in older versus younger adults: An important sensory role for right putamen. *Human Brain Mapping*, *33*, 895–908.
- Graziano, M. S., & Gross, C. G. (1998). Spatial maps for the control of movement. *Current Opinion in Neurobiology*, *8*(2), 195–201.
- Greenspan, J. D., & Winfield, J. A. (1992). Reversible pain and tactile deficits associated with a cerebral tumor compressing the posterior insula and parietal operculum. *Pain*, *50*(1), 29–39.
- Han, J., Waddington, G., Adams, R., Anson, J., & Liu, Y. (2016). Assessing proprioception: A critical review of methods. *Journal of Sport and Health Science*, *5*(1), 80–90.
- Herwig, U., Satrapi, P., & Schönfeldt-Lecuona, C. (2003). Using the international 10–20 EEG system for positioning of transcranial magnetic stimulation. *Brain Topography*, *16*(2), 95–99.
- Iandolo, R., Bellini, A., Saiote, C., Marre, I., Bommarito, G., Oesingmann, N., ... Inglese, M. (2018). Neural correlates of lower limbs proprioception: An fMRI study of foot position matching. *Human Brain Mapping*, *39*(5), 1929–1944.
- Jones, S. A., Fiehler, K., & Henriques, D. Y. (2012). A task-dependent effect of memory and hand-target on proprioceptive localization. *Neuropsychologia*, *50*, 1462–1470.
- Kenzie, J. M., Ben-Shabat, E., Lamp, G., Dukelow, S. P., & Carey, L. M. (2018). Illusory limb movements activate different brain networks than imposed limb movements: An ALE meta-analysis. *Brain Imaging and Behavior*, *12*(4), 919–930.
- Kenzie, J. M., Findlater, S. E., Pittman, D. J., Goodyear, B. G., & Dukelow, S. P. (2019). Errors in proprioceptive matching post-stroke are associated with impaired recruitment of parietal, supplementary motor, and temporal cortices. *Brain Imaging and Behavior*, 1–15. <https://doi.org/10.1007/s11682-019-00149-w>
- Lashley, K. S. (2017). The accuracy of movement in the absence of excitation from the moving organ. *American Journal of Physiology*, *43*, 169–194.
- Makeig, S. (1993). Auditory event-related dynamics of the EEG spectrum and effects of exposure to tones. *Electroencephalography and Clinical Neurophysiology*, *86*(4), 283–293.
- Makeig, S., Debener, S., Onton, J., & Delorme, A. (2004). Mining event-related brain dynamics. *Trends in Cognitive Sciences*, *8*(5), 204–210.
- Marini, F., Ferrantino, M., & Zenzeri, J. (2018). Proprioceptive identification of joint position versus kinaesthetic movement reproduction. *Human Movement Science*, *62*, 1–13.
- Marini, F., Squeri, V., Morasso, P., Konczak, J., & Masia, L. (2016). Robot-aided mapping of wrist proprioceptive acuity across a 3D workspace. *PLoS One*, *11*(8), e0161155.
- Marini, F., Squeri, V., Morasso, P., & Masia, L. (2016). Wrist proprioception: Amplitude or position coding? *Frontiers in Neurorobotics*, *10*, 1–8.

- Marshall, J. (1951). Sensory disturbances in cortical wounds with special reference to pain. *Journal of Neurology, Neurosurgery, and Psychiatry*, 14(3), 187–204.
- McFarland, D. J., Miner, L. A., Vaughan, T. M., & Wolpaw, J. R. (2000). Mu and Beta rhythm topographies during motor imagery and actual movements. *Brain Topography*, 12(3), 177–186.
- Mesulam, M.-M. (1981). A cortical network for directed attention and unilateral neglect. *Annals of Neurology*, 10(4), 309–325.
- Mohan, V., Bhat, A., & Morasso, P. (2018). Muscleless motor synergies and actions without movements: From motor neuroscience to cognitive robotics. *Physics of Life Reviews*. <https://doi.org/10.1016/j.plrev.2018.04.005> [Epub ahead of print]
- Naito, E. (2004). Sensing limb movements in the motor cortex: How humans sense limb movement. *Neuroscience*, 10(1), 73–82.
- Naito, E., Nakashima, T., Kito, T., Aramaki, Y., Okada, T., & Sadato, N. (2007). Human limb-specific and non-limb-specific brain representations during kinesthetic illusory movements of the upper and lower extremities. *The European Journal of Neuroscience*, 25, 3476–3487.
- Naito, E., Roland, P. E., Grefkes, C., Choi, H. J., Eickhoff, S., Geyer, S., ... Ehrsson, H. H. (2005). Dominance of the right hemisphere and role of area 2 in human kinesthesia. *Journal of Neurophysiology*, 93(2), 1020–1034.
- Neuper, C., Scherer, R., Reiner, M., & Pfurtscheller, G. (2005). Differential effects of kinesthetic and visual-motor mode of imagery in single-trial EEG. *Cognitive Brain Research*, 25(3), 668–677.
- Niedermeyer, E. (1997). Alpha rhythms as physiological and abnormal phenomena. *International Journal of Psychophysiology*, 26(1–3), 31–49.
- Oldfield, R. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, 9(1), 97–113.
- Orban de Vivry, J.-J., Legrain, V., & Lefèvre, P. (2017). Overlap of movement planning and movement execution reduces reaction time. *Journal of Neurophysiology*, 117(1), 117–122.
- Pfurtscheller, G., & Aranibar, A. (1979). Evaluation of event-related desynchronization (ERD) preceding and following voluntary self-paced movement. *Electroencephalography and Clinical Neurophysiology*, 46(2), 138–146.
- Pfurtscheller, G., Neuper, C., Andrew, C., & Edlinger, G. (1997). Foot and hand area mu rhythms. *International Journal of Psychophysiology*, 26(1–3), 121–135.
- Proske, U. (2006). Kinesthesia: The role of muscle receptors. *Muscle & Nerve*, 34(5), 545–558.
- Proske, U., & Gandevia, S. C. (2009). The kinaesthetic senses. *The Journal of Physiology*, 587(Pt 17), 4139–4146.
- Proske, U., & Gandevia, S. C. (2012). The proprioceptive senses: Their roles in signaling body shape, body position and movement, and muscle force. *Physiological Reviews*, 92(4), 1651–1697.
- Raspopovic, S., Capogrosso, M., Petrini, F. M., Bonizzato, M., Rigosa, J., Di Pino, G., ... Micera, S. (2014). Restoring natural sensory feedback in real-time bidirectional hand prostheses. *Science Translational Medicine*, 6(222), 222ra19–222ra19.
- Restuccia, D., Valeriani, M., Barba, C., Le Pera, D., Bentivoglio, A., Albanese, A., ... Tonali, P. (2003). Abnormal gating of somatosensory inputs in essential tremor. *Clinical Neurophysiology*, 114(1), 120–129.
- Rinderknecht, M. D., Popp, W. L., Lambercy, O., & Gassert, R. (2016). Reliable and rapid robotic assessment of wrist proprioception using a gauge position matching paradigm. *Frontiers in Human Neuroscience*, 10, 316.
- Rizzolatti, G., Luppino, G., & Matelli, M. (1998). The organization of the cortical motor system: New concepts. *Electroencephalography and Clinical Neurophysiology*, 106(4), 283–296.
- Sainburg, R. L., Ghilardi, M. F., Poizner, H., & Ghez, C. (1995). Control of limb dynamics in normal subjects and patients without proprioception. *Journal of Neurophysiology*, 73(2), 820–835.
- Schabrun, S. M., & Hillier, S. (2009). Evidence for the retraining of sensation after stroke: A systematic review. *Clinical Rehabilitation*, 23(1), 27–39.
- Scott, S. H. (2012). The computational and neural basis of voluntary motor control and planning. *Trends in Cognitive Sciences*, 16, 541–549.
- Seiss, E., Hesse, C. W., Drane, S., Oostenveld, R., Wing, A. M., & Praamstra, P. (2002). Proprioception-related evoked potentials: Origin and sensitivity to movement parameters. *NeuroImage*, 17(1), 461–468.
- Seiss, E., Praamstra, P., Hesse, C., & Rickards, H. (2003). Proprioceptive sensory function in Parkinson's disease and Huntington's disease: Evidence from proprioception-related EEG potentials. *Experimental Brain Research*, 148(3), 308–319.
- Sherrington, C. S. (1907). On the Proprioceptive system, especially in its reflex aspect. *Brain*, 29(4), 467–482.
- Sober, S. J., & Sabes, P. N. (2003). Multisensory integration during motor planning. *The Journal of Neuroscience*, 23(18), 6982–6992.
- Sullivan, J. E., & Hedman, L. D. (2008). Sensory dysfunction following stroke: Incidence, significance, examination, and intervention. *Topics in Stroke Rehabilitation*, 15(3), 200–217.
- Szurhaj, W., Derambure, P., Labyt, E., Cassim, F., Bourriez, J.-L., Isnard, J., ... Mauguière, F. (2003). Basic mechanisms of central rhythms reactivity to preparation and execution of a voluntary movement: A stereoelectroencephalographic study. *Clinical Neurophysiology*, 114(1), 107–119.
- Tabot, G. A., Kim, S. S., Winberry, J. E., & Bensmaia, S. J. (2015). Restoring tactile and proprioceptive sensation through a brain interface. *Neurobiology of Disease*, 83, 191–198.
- Taub, E., Goldberg, I. A., & Taub, P. (1975). Deafferentation in monkeys: Pointing at a target without visual feedback. *Experimental Neurology*, 46(1), 178–186.
- ter Horst, A. C., Cole, J., van Lier, R., & Steenbergen, B. (2012). The effect of chronic deafferentation on mental imagery: A case study. *PLoS One*, 7(8), e42742.
- Tsakiris, M., Hesse, M. D., Boy, C., Haggard, P., & Fink, G. R. (2007). Neural signatures of body ownership: A sensory network for bodily self-consciousness. *Cerebral Cortex*, 17(10), 2235–2244.
- Tsay, A. J., Giummarra, M. J., Allen, T. J., & Proske, U. (2016). The sensory origins of human position sense. *The Journal of Physiology*, 594(4), 1037–1049.
- van Beers, R. J., Sittig, A. C., & van der Gon, J. J. D. (1999). Integration of proprioceptive and visual position-information: An experimentally supported model. *Journal of Neurophysiology*, 81(3), 1355–1364.
- Volpe, B. T., LeDoux, J. E., & Gazzaniga, M. S. (1979). Spatially oriented movements in the absence of proprioception. *Neurology*, 29(9 Pt 1), 1309–1313.
- Weiller, C., Jüptner, M., Fellows, S., Rijntjes, M., Leonhardt, G., Kiebel, S., ... Thilmann, A. F. (1996). Brain representation of active and passive movements. *NeuroImage*, 4(2), 105–110.

How to cite this article: Marini F, Zenzeri J, Pippo V, Morasso P, Campus C. Neural correlates of proprioceptive upper limb position matching. *Hum Brain Mapp*. 2019;40: 4813–4826. <https://doi.org/10.1002/hbm.24739>