UNIVERSITY OF GENOVA

PhD PROGRAM IN BIOENGINEERING AND ROBOTICS

Neural and motor basis of inter-individual interactions

by

Pauline HILT

Thesis submitted for the degree of Doctor of Philosophy (31° cycle)

December 2018

Prof. Alessandro D'Ausilio, Prof. Thierry Pozzo,   Supervisors

Dr. Alberto Inuggi

Thesis Jury:

Prof. Avenanti A., University of Bologna   External examiner

Prof. Cattaneo L., University of Verona   External examiner

Dibris

Department of Informatics, Bioengineering, Robotics and Systems Engineering

Declaration

I hereby declare that except where specific reference is made to the work of others, the contents of this dissertation are original and have not been submitted in whole or in part for consideration for any other degree or qualification in this, or any other university. This dissertation is my own work and contains nothing which is the outcome of work done in collaboration with others, except as specified in the text and Acknowledgements. This dissertation contains fewer than 65,000 words including appendices, bibliography, footnotes, tables and equations and has fewer than 150 figures.

Pauline HILT

December 2018

Acknowledgements

Synopsis

The goal of my Ph.D. work was to investigate the behavioral markers and the brain activities responsible for the emergence of sensorimotor communication. Sensorimotor communication can be defined as a form of communication consisting into flexible exchanges based on bodily signals, in order to increase the efficiency of the inter-individual coordination. For instance, a soccer player carving his movements to inform another player about his intention. This form of interaction is highly dependent of the motor system and the ability to produce appropriate movements but also of the ability of the partner to decode these cues.

To tackle these facets of human social interaction, we approached the complexity of the problem by splitting my research activities into two separate lines of research.

First, we pursued the examination of motor-based humans' capability to perceive and "read" other's behaviors in focusing on single-subject experiment. The discovery of mirror neurons in monkey premotor cortex in the early nineties (di Pellegrino et al. 1992) motivated a number of human studies on this topic (Rizzolatti and Craighero 2004). The critical finding was that some ventral premotor neurons are engaged during visual presentation of actions performed by conspecifics. More importantly, those neurons were shown to encode also the actual execution of similar actions (i.e. irrespective of who the acting individual is). This phenomenon has been highly investigated in humans by using cortical and cortico-spinal measures (for review see, fMRI: Molenberghs, Cunnington, and Mattingley 2012; TMS: Naish et al. 2014; EEG: Pineda 2008).

During single pulse TMS (over the primary motor cortex), the amplitude of motor evoked potentials (MEPs) provides an index of corticospinal recruitment. During action observation the modulation of this index follow the expected changes during action execution (Fadiga et al. 1995). However, dozens of studies have been published on this topic and revealed important inconsistencies. For instance, MEPs has been shown to be dependent on observed low-level motor features (e.g. kinematic features or electromyography temporal coupling; Gangitano, Mottaghy, and Pascual-Leone 2001; Borroni et al. 2005; Cavallo et al. 2012) as well as high level movement properties (e.g. action goals; Cattaneo et al. 2009; Cattaneo et al. 2013). Furthermore, MEPs modulations do not seem to be related to the observed effectors (Borroni and Baldissera 2008; Finisguerra et al. 2015; Senna, Bolognini, and Maravita 2014), suggesting their independence from low-level movement features.

These contradictions call for new paradigms. Our starting hypothesis here is that the organization and function of the mirror mechanism should follow that of the motor system during action execution. Hence, we derived three action observation protocols from classical motor control theories:

1) The first study was motivated by the fact that motor redundancy in action execution do not allow the presence of a one-to-one mapping between (single) muscle activation and action goals. Based on that, we showed that the effect of action observation (observation of an actor performing a power versus a precision grasp) are variable at the single muscle level (MEPs; motor evoked potentials) but robust when evaluating the kinematic of TMS-evoked movements. Considering that movements are based on the coordination of multiple muscle activations (muscular synergies), MEPs may represent a partial picture of the real corticospinal activation. Inversely, movement kinematics is both the final functional byproduct of muscles coordination and the sole visual feedback that can be extracted from action observation (i.e. muscle recruitment is not visible). We conclude that TMS-evoked kinematics may be more reliable in representing the state of the motor system during action observation.

2) In the second study, we exploited the inter-subject variability inherent to everyday whole-body human actions, to evaluate the link between individual motor signatures (or motor styles) and other's action perception. We showed no group-level effect but a robust correlation between the individual motor signature recorded during action execution and the subsequent modulations of corticospinal excitability during action observation. However, results were at odds with a strict version of the direct matching hypothesis that would suggest the opposite pattern. In fact, the more the actor's movement was similar to the observer's individual motor signature, the smaller was the MEPs amplitude, and vice versa. These results conform to the predictive coding hypothesis, suggesting that during AO, the motor system compares our own way of doing the action (individual motor signature) with the action displayed on the screen (actor's movement).

3) In the third study, we investigated the neural mechanisms underlying the visual perception of action mistakes. According to a strict version of the direct matching hypothesis, the observer should potentially reproduce the neural activation present during the actual execution of action errors (van Schie et al. 2004). Here, instead of observing an increase of cortical inhibition, we showed an early (120 ms) decrease of intracortical inhibition (short intracortical inhibition) when a mismatch was present between the observed action (erroneous) and the observer's expectation. As proposed by the predictive coding framework, the motor system may be

involved in the generation of an error signal potentially relying on an early decrease of intracortical inhibition within the corticomotor system.

The second line of research aimed at the investigation of how sensorimotor communication flows between agents engaged in a complementary action coordination task. In this regard, measures of interest where related to muscle activity and/or kinematics as the recording of TMS-related indexes would be too complicated in a joint-action scenario.

1) In the first study, we exploited the known phenomenon of Anticipatory Postural Adjustments (APAs). APAs refers to postural adjustments made in anticipation of a self- or externally-generated disturbance in order to cope for the predicted perturbation and stabilize the current posture. Here we examined how observing someone else lifting an object we hold can affect our own anticipatory postural adjustments of the arm. We showed that the visual information alone (joint action condition), in the absence of efference copy (present only when the subject is unloading by himself the object situated on his hand), were not sufficient to fully deploy the needed anticipatory muscular activations. Rather, action observation elicited a dampened APA response that is later augmented by the arrival of tactile congruent feedback.

2) In a second study, we recorded the kinematic of orchestra musicians (one conductor and two lines of violinists). A manipulation was added to perturb the normal flow of information conveyed by the visual channel. The first line of violinist where rotated 180°, and thus faced the second line. Several techniques were used to extract inter-group (Granger Causality method) and intra-group synchronization (PCA for musicians and autoregression for conductors). The analyses were directed to two kinematic features, hand and head movements, which are central for functionally different action. The hand is essential for instrumental actions, whereas head movements encode ancillary expressive actions. During the perturbation, we observed a complete reshaping of the whole patterns of communication going in the direction of a distribution of the leadership between conductor and violinists, especially for what regards head movements. In fact, in the perturbed condition, the second line acts as an informational hub connecting the first line to the conductor they no longer can see. This study evidences different forms of communications (coordination versus synchronization) flowing via different channels (ancillary versus instrumental) with different time-scales.

Table of Contents

Abbreviations

TMS: Transcranial Magnetic Stimulation

AON: Action Observation Network

MEP: Motor-Evoked Potentials

MEK: whole-hand TMS Evoked Kinematics

cTBS: continuous Theta Burst Stimulation

CSE: Corticospinal Excitability (CSE)

AOE: Action Observation Effects

EMG: Electromyography

FDI: First Dorsal Interosseus

ADM: Abductor Digiti Minimi

FLX: arm Flexor Digitorum Superficialis

EDC: Extensor Digitorum

rMT: resting Motor Threshold

aMT: active Motor Threshold

EEG: Electroencephalography

MEG: Magnetoencephalography

fMRI: Functional Magnetic Resonance Imaging

M1: Primary motor cortex

PCA: principal component analysis

PC: principal component

PC1%: percentage of variance explained by the first PC

pow: power grasping

prec: precision grasping

IMS: Individual Motor Signature

AE: Action Execution

AO: Action Observation

TA: Tibialis Anterior

SO: Soleus

RMSE: root mean squared error

Dist_ankle: kinematic distance to ankle stimulus

Dist_knee: kinematic distance to knee stimulus

ERN: EEG error-related negativity

NMDA: N-methyl-D-aspartate

ICF: Intracortical Facilitation

sICI: short Intracortical Inhibition

spTMS: single pulse TMS

ppTMS: paired pulse TMS

ISI: Inter-Stimuli Interval

RT: Reaction Time

iMEP: index of intracortical modulation

GABAa: Gamma-Aminobutyric acid

APA: Anticipatory Postural Adjustment

EO: eyes opened

EC: eyes closed

ToC: Time of Contact

Lon: Lift onset

Loff: Lift offset

FDS: wrist flexor

EXT: wrist extensor

Vfb: Visual feedback

Tfb: Touch feedback

Ffb: Force feedback

ECopy: Efference Copy

Mon: Movement onset

SEM: standard error of the mean

S1: first section of violinists

S2: second section of violinists

C: conductor of the orchestra

VX: violinist number X

CX: conductor number X

ARfit: conductor behavior predictability (goodness of fit of the associated auto-regressive model)

Norm: normal

Pert: perturbed

G-causes: Granger-causes

Gca: Granger-causality score

GX->Y or X->Y: gca of X on Y

VAF: variance accounted for

CSP: Cortical Silent Periods

CoM: Center of Mass

List of figures

List of supplementary materials

General introduction

Social interaction is an essential part of human's everyday life. By moving our own body and in parallel perceiving other's behavior we can communicate in various contexts like speaking at the phone, shaking hands, smiling to a passerby or playing music. These forms of interaction rely on sensorimotor communication. Sensorimotor communication is a form of communication that consists into flexible exchanges of bodily signals, to promote an efficient coordination. This form of communication is highly dependent of the motor system and the ability to produce appropriate movements but also of the ability of the partner to decode these cues (Pezzulo et al. 2018).

For methodological reasons, the neurophysiological study of sensorimotor communication has first been done by examining isolated individuals engaged in simulated social context. In these contexts, many studies investigated the fundamental ability to predict and adapt to incoming perceptual information about other's behaviour.

Observing others' actions activates brain areas (Action Observation Network - AON) including premotor and inferior parietal regions (inferior frontal (IFC), anterior intraparietal (AIP), superior temporal sulcus (STS) and somatosensory cortices (S1)) partially overlapping with those recruited for action preparation and execution (Giese and Rizzolatti 2015). Many studies in humans have in the last 20 years attempted to identify brain regions having what have been defined "mirror properties". This lead to broad and sometimes speculative claims about their role in social cognition (Molenberghs, Cunnington, and Mattingley 2012). In fact, the neural substrates of mirror activities remain controversial.

More particularly, using Transcranial Magnetic Stimulation (TMS), about 100 studies have shown that corticospinal excitability (CSE), via Motor Evoked Potentials (MEPs) modulation, maps action execution features during observation (Fadiga et al. 1995; Fadiga, Craighero, and Olivier 2005; Naish et al. 2014). Some studies show that MEPs are modulated by observation of movement features (low-level features), for example the kinematic features (finger aperture in a grasping action; Gangitano, Mottaghy, and Pascual-Leone 2001), the amplitude of muscle activity over time (Borroni et al. 2005; Cavallo et al. 2012) or the forces needed (lift objects of different weights; Alaerts et al. 2010; Senot et al. 2011). Other reports show that MEPs are modulated by action goals (Cattaneo et al. 2009; Cattaneo et al. 2013; high-level features). For instance, MEPs modulation do not seem to depend on the effector used to attain the same object grasping goal (Borroni and Baldissera 2008; Senna, Bolognini, and Maravita 2014; Finisguerra et al. 2015), suggesting independence from low-level movement features. Lastly, studies trying to separate these dimensions, highlight the multi-

dimensionality of the Action Observation Effect (AOE), dependent on the details of the experimental setup such as instructions (Mc Cabe et al. 2014; Sartori et al. 2015), TMS trigger timing (Cavallo et al. 2013) and recorded muscles (Betti, Castiello, and Sartori 2015). Additionally, external influences like learning (Catmur, Walsh, and Heyes 2007; Catmur et al. 2008) or context (Brass et al. 2007) modulate AOEs. The large variability and incongruence regarding AOEs questions fundamental methodological and theoretical aspects of how to best take advantage of TMS in this field. In this regard, two major explanatory models currently coexist bringing in many cases to opposite predictions.

The direct matching hypothesis (Rizzolatti, Fogassi, and Gallese 2001; Rizzolatti and Craighero 2004) is based on the idea that action observation activates the neurons that represent this action in the observer's premotor cortex. These activations induce automatically a motor representation of the observed action corresponding to the one spontaneously generated during action execution. On this basis, general action outcomes become accessible to the observer as if he was himself acting. This hypothesis is based on neurophysiological evidences that perception and execution of actions show an important degree of neurobehavioral overlap (e.g. common feature; Borroni et al. 2005; Cattaneo et al. 2013; Gangitano, Mottaghy, and Pascual-Leone 2001; Hilt et al. 2017; Kilner and Lemon 2013; Naish et al. 2014; Rizzolatti and Sinigaglia 2016). In agreement with such claims, perceiving actions out of the observer's motor abilities (e.g. a dog barking) did not activate motor structures, unlike actions present in the motor repertoire (e.g. biting done by a dog or a human; Buccino et al. 2004). These results might be the proof of a direct match occurring between observed and executed actions based on what the observer can extract from a visual description of other's actions.

Differently, the predictive-coding approach suggests that "reading" other's actions stem from an empirical Bayesian inference process, in which top-down expectations (e.g. goal) allow the prediction of lower level of action representation (e.g. motor commands; Kilner, Friston, and Frith 2007). Predicted motor commands are compared with observed kinematics to generate a prediction error that is further propagated across cortical levels to update information according to the actual outcome. Motor activities during perception are indeed modulated by higher-order information (e.g. prior knowledge or contextual cues; Amoruso and Urgesi 2016; Cretu et al. 2018; Hudson et al. 2016). In this perspective, an increase of activity in the action observation network reflects the computation of a larger error between predicted and currently perceived movements, instead of an exact match.

We propose that these controversies arise from a poorly defined description of what the activity of the motor cortex, as well as motion kinematics and muscle level representation, should look like during action execution. In other terms, the difficulties in understanding the mirror coding may

directly stem from which level of description we adopt when modeling the function of the motor system.

The works presented in the first part will show different approaches based on classical motor control theories (muscular synergies and individual motor signatures) to allow a deeper understanding of sensorimotor activities during action observation.

Furthermore, resolving these issues may be of great importance to tackle human's ability to efficiently interact together. Indeed, others' action discrimination may serve a social role in rapidly preparing an appropriate answer. One key function of the AON could be that of supporting temporal and spatial interpersonal coordination, as for joint actions (JA; Sebanz, Bekkering, and Knoblich 2006). In fact, we need to observe other's actions, to produce complementary responses in a turn-taking fashion (e.g., playing tennis) or to smoothly and simultaneously coordinate our own movement with the one of others (e.g., when moving a heavy object together). Following the predictive coding hypothesis, fast coordination in an interactive scenario may be achieved by building an internal predictive model of the partner(s) behavior and compare it with the current observed movement, to generate a prediction error (Friston, Mattout, and Kilner 2011) and update the ongoing motor planning (Sebanz, Bekkering, and Knoblich 2006).

In this regard, a first body of literature investigated how dyads achieve interpersonal simple sensorimotor coordination, such as walking side-by-side (van Ulzen et al. 2008), rocking in rocking-chairs (Richardson et al. 2007) or coordinating finger movements (Repp 2005; Oullier et al. 2008). In such contexts, co-actors continuously influence each other and tend to spatially and temporally synchronize their movements - even unintentionally (Richardson et al. 2007; van Ulzen et al. 2008). However, social interaction goes beyond synchronization with other's actions and relies also on inferring others' motor goals and intentions to generate a context-appropriate action. Interestingly, activity of the AON differentiates between AO to imitate and AO to generate a complementary response (Newman-Norlund, van Schie, et al. 2007; Sartori and Betti 2015), with the initial imitative reaction being suppressed by a self-generated and context-appropriate response (Brass et al., 2005; Cross et al., 2013; Longo et al., 2008; Sartori et al., 2012). Collaborative actions may also indirectly recruit the mirror neuron system, to relate observed and executed actions and then use this matching to support complementary actions planning.

The role of mirror like phenomena in complementary actions may be approached by examining the phenomenon of motor contagion (or automatic imitation). Automatic imitation is the involuntarily tendency to reproduce specific movement features of the interacting partner (i.e. of the observed action). For instance, participants' movements are automatically contaminated by the velocity profile

of an interacting partner (in building a tower; (D'Ausilio, Badino, et al. 2015) or a moving dot (Bisio et al. 2010) in respectively ballistic reaching or rhythmic movements. This automatic motor contagion decreased when the interacting partner violates the biological laws of motion (i.e. bellshaped velocity profile; Bisio et al. 2014). These findings highlight the existence of a sensory-motor matching mechanism, at a very low-level, that may form the basis upon which higher levels of social interaction could be built (e.g. by facilitating group behavioral entrainment; Dumas, Laroche, and Lehmann 2014).

The works presented in the second part examine how sensory information modulates in real-time different types of complex sensorimotor interactions.

Part 1. Action Observation

1. **Study 1: Action observation effects reflect the modular organization of the human motor system**

Action observation, similarly, to action execution, facilitates the observer's motor system and Transcranial Magnetic Stimulation (TMS) has been instrumental in exploring the nature of these motor activities. However, contradictory findings question some of the fundamental assumptions regarding the neural computations run by the Action Observation Network (AON). To better understand this issue, we delivered TMS over the observers' motor cortex at two timings of two reaching-grasping actions (precision vs power grip) and we recorded Motor-Evoked Potentials (4 hand/arm muscles; MEPs). At the same time, we also recorded whole-hand TMS Evoked Kinematics (8 hand elevation angles; MEKs) that capture the global functional motor output, as opposed to the limited view offered by recording few muscles. By repeating the same protocol twice, and a third time after continuous theta burst stimulation (cTBS) over the motor cortex, we observe significant time-dependent grip-specific MEPs and MEKs modulations, that disappeared after cTBS. MEKs, differently from MEPs, exhibit a consistent significant modulation across pre-cTBS sessions. Beside clear methodological implications, the multidimensionality of MEKs opens a window on muscle synergies needed to overcome system redundancy. By providing better access to the AON computations, our results strengthen the idea that action observation shares key organizational similarities with action execution.

My Contribution: data analysis, results interpretation and manuscript writing

This work was published in Cortex:

PM Hilt, E Bartoli, E Ferrari, M Jacono, L Fadiga and A D'Ausilio (2017) Action observation effects reflect the modular organization of the human motor system. Cortex, 95: 104-118

This work has been presented as on oral communication in the Brain Stimulation and Imaging Meeting (24 and 25 june, 2016, Geneva, Switzerland):

PM Hilt, E Bartoli, E Ferrari and A D'Ausilio. The role of the motor cortex in action observation: a cTBS study

Action execution and action observation evoke similar activities in the human brain (Rizzolatti and Sinigaglia 2016). However, there is a considerable debate around the specificity and purposes of action observation-evoked motor facilitation (D'Ausilio, Bartoli, and Maffongelli 2015a).

Dozens of studies have been published using Transcranial Magnetic Stimulation (TMS) and Motor Evoked Potentials (MEPs) to investigate how modulations of corticospinal excitability (CSE), during action observation, reflect action execution features (Fadiga et al. 1995; Fadiga, Craighero, and Olivier 2005; Naish et al. 2014). Some studies show that MEPs are modulated by observation of low-level motor features, such as kinematic features (e.g. fingers aperture during grasping action, Gangitano et al., 2001), EMG temporal coupling (Borroni et al. 2005; Cavallo et al. 2012) or forces (observation of lifting of objects of different weight, Alaerts et al., 2010; Senot et al., 2011). Others works report higher level modulations, such as action goals (Cattaneo et al., 2009, 2013; high-level features). For instance, MEPs modulations do not seem to depend on the effector used in the observation of the same object grasping goal (Senna, Bolognini, and Maravita 2014; Finisguerra et al. 2015; Borroni and Baldissera 2008), suggesting their independence from low-level movement features. Lastly, studies trying to separately analyse these aspects, highlight the multi-dimensionality of Action Observation Effects (AOEs), which may depend on several details of the experimental protocol such as instructions (Mc Cabe et al. 2014; Sartori et al. 2015), TMS trigger timing (Cavallo et al. 2013) and number of recorded muscles (Betti, Castiello, and Sartori 2015). External influences such as learning (Catmur, Walsh, and Heyes 2007; Catmur et al. 2008) or context (Brass et al. 2007) may modulate AOEs as well.

However, apart from identifying key features of the AOEs, these studies rarely tested the reproducibility of their effects. In fact, MEPs are highly variable across time (S. Schmidt et al. 2009) and hugely dependent on cortical states (Klein-Flügge et al. 2013) and on spontaneous cortical oscillatory dynamics (Elswijk et al. 2010; Keil et al. 2014). More importantly, in many cases MEPs might not be the most accurate measure to explore AOEs. In fact, one basic tenet of action observation studies is that the visual appearance of actions is directly mapped onto one unique muscle activity pattern. Based on this assumption, CSE is usually recorded from few muscles at a time, during the observation of often complex kinematic configurations. CSE modulations are then used to build inferences about the functional meaning of motor activities during action observation (Naish et al. 2014). However, it is known that the same kinematic configuration can be achieved via largely different underlying muscle activation patterns (Levin et al. 2003; Grasso, Bianchi, and Lacquaniti 1998).

Here we suggest that the TMS-evoked kinematic pattern (Motor Evoked Kinematics, MEK) provides a more reliable measure of motor activities induced by action observation. This assumption is based on principles of redundancy and invariance during motor execution (Sporns and Edelman 1993; Flash and Hochner 2005; Guigon, Baraduc, and Desmurget 2007) and it takes into account the fact that the control of grasping actions relies upon the composition of intracortical, corticospinal, spinal and peripheral influences (Fetz et al. 2002) which in turn regulate the temporal-spatial coordination of multiple agonist and antagonist muscles.

The functional output of the motor system can be extrapolated from TMS-induced MEK (Finisguerra et al. 2015; Gentner and Classen 2006; Bartoli et al. 2014). Single finger MEKs are modified by physical practice (Classen et al. 1998) and by action observation training (Celnik et al. 2006; Stefan et al. 2005; Stefan et al. 2008) thus reflecting short-term cortical plasticity. Whole-hand MEKs replicate the modular organization of hand functions, which are dissociable in discrete postures (Gentner and Classen 2006), requiring years of practice to be significantly changed (Gentner et al. 2010). Importantly, MEKs offer a direct measure of the functional motor output, without losing its inherent multidimensionality. This fact may have a significant impact on how we investigate the nature of AOEs (D'Ausilio, Bartoli, and Maffongelli 2015a) and could clarify to what extent action observation and action execution share similar synergistic organization principles.

To this end, we compared side-by-side MEPs and MEKs in a classical action observation protocol. Subjects observed a goal directed grasping action towards one of two simultaneously presented objects, requiring either a precision or a power grip. We recorded MEPs from 4 hand muscles as well as whole-hand MEKs at one of two possible time points during the observed reaching phase. The first time-point corresponds to maximal wrist acceleration, when limited cues are available to predict which object is going to be grasped. The second one was temporally aligned to maximal wrist velocity, occurring during the fingers opening phase, a moment at which the action goal becomes predictable (Gangitano, Mottaghy, and Pascual-Leone 2001). The experimental design replicates the same paradigm to evaluate the reproducibility of the AOEs. On day one, the action observation protocol was measured alone, on the second day the action observation protocol was repeated before administering continuous Theta Burst Stimulation (cTBS) over the primary motor cortex. The action observation was then repeated a third time after cTBS administration to evaluate a potential causal contribution of M1 excitability to both measures, MEPs and MEKs. Beside important considerations about the replicability of MEKs and MEPs, results will nourish theoretical considerations about the way by which action observation-induced motor facilitation reflects the functional, synergistic organization of the motor output.

(b)   Material and methods

<u>Participants</u>

Fifteen volunteers (5 males, 10 females, mean age 25.4 ± 3.41 years (m±sd)) participated in the study. All participants were right handed (Edinburgh handedness inventory ; Oldfield, 1971), with normal or corrected to normal vision and no contraindication to TMS according to their personal clinical history. None of them reported after-TMS undesired effects. The whole experimental procedure was approved by the local ethics committee and was in compliance with National legislation and the Code of Ethical Principles for Medical Research Involving Human Subjects of the World Medical Association (Declaration of Helsinki). Participants gave their informed consent before performing the experiment and were remunerated for their participation.

<u>Stimuli</u>

During the whole experiment, subjects sat on a TMS chair (Rogue Research Inc., Montreal, Quebec), with their elbow flexed at 90° and their hand prone in a relaxed position. Their head was kept stable via a chin and a head rest. The stimuli, two video-clips of reach-to-grasp actions, were displayed through Psychtoolbox-3 software (PTB-3, The MathWorks Inc., Natick, MA, USA), on a computer screen placed in front of the subject (distance of 60 cm). Clips were recorded via a Sony 3D camera (Sony Corporation, Tokyo, Japan) at the format of 800x600 pixel and length of 2500ms. Each clip showed an actor reaching either one of two different objects, simultaneously present on a table. The distance between the hand resting position and the objects was about 50 cm. The two objects were a small sphere (diameter 2 cm; graspable by precision grip) and a large sphere (diameter 10 cm; graspable by power grip). The two objects were placed on a table at a small distance from each other (10 cm) to create an ambiguity regarding the final target of the grasping action. Actions were shown from a lateral perspective to maximize the visibility of hand trajectory and finger opening but making it difficult to predict the action goal. The two video-clips (one for each object) were selected from a set of 40 video-clips of the same actor reaching for the small sphere (half of the trials) or the large one. During these video recordings, we also captured movement kinematics and electromyography (EMG) of the actor. This information was used to select two movies with similar duration and similar kinematic features (e.g. wrist velocity and grip aperture, Figure 1B). A more detailed description of kinematic and EMG recording of the stimuli are available in Supplementary Material B.
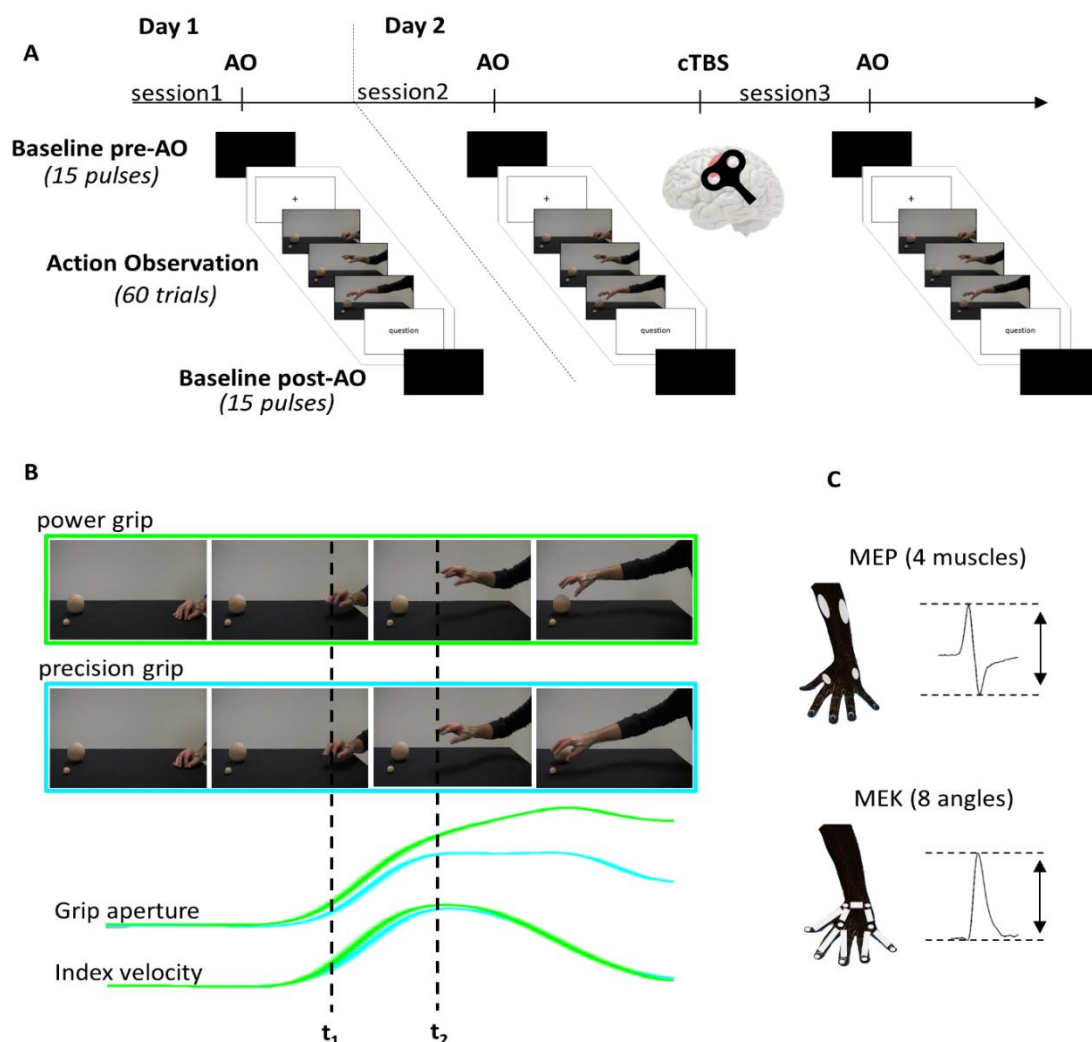
Figure 1: Illustration of the experimental protocol, stimuli and dependent variables.
A. Time course of the experiment across the two days, showing the 3 sessions (session 1 − day 1, session 2 − day $2_{pre\text{-}cTBS}$ and session 3 − day $2_{post\text{-}cTBS}$) each starting with a baseline (baseline$_{pre}$), followed by an action observation run (AO) and a second baseline recording (baseline$_{post}$). The cTBS protocol was applied on day 2 (between session 2 and session 3). B. Four representative frames of the two displayed movies (upper panel: power grip, lower panel: precision grip) and associated kinematic (grip aperture and index velocity). Timing t_1 and t_2 are represented by black dotted vertical lines. C. Typical recording for MEPs (four muscles: FDI, ADM, EDC and FLX) and MEKs (8 elevation angles: thumb, index, middle finger, ring finger, 5th finger, index knuckle, 5th finger knuckle, and wrist). In the present study, we used the peak to peak amplitude for both measures.

Procedure

All subjects completed three experimental sessions over two different days (Figure 1A). During the first day, they performed one experimental run of the action observation protocol (session 1 − day 1). In the second day, the participants completed two experimental runs of the same action observation protocol: one session before (session 2 − day $2_{pre\text{-}cTBS}$) and one after (session 3 − day $2_{post\text{-}cTBS}$) the application of continuous theta burst stimulation (cTBS) over the left primary motor cortex (see the

TMS section for more details). Each day started with the TMS mapping procedure (see the TMS section for more details). Each action observation run started with 15 baseline trials with the subject at rest (baseline$_{pre}$). After the baseline, subjects completed 60 action observation trials (30 trials for each object type, precision and power), followed again by 15 baseline trials (baseline$_{post}$). Each action observation trial began with a fixation cross on the computer screen. After an inter-trial interval (varying from 8 to 12 seconds) the fixation cross disappeared and the movie started. In one third of the trials, subjects were asked if the action just presented was the same as the previous one (to monitor attention). The two first sessions lasted about 30 minutes, and the third session lasted about 50 minutes, including subject preparation, debriefing, and cTBS application (only for the third session). On average the time elapsed between session 1 and 2 was 6 days (+/1.2 days (STD)). The time of the day was kept as constant as possible: it was the same for 10 subjects, while for the remaining participants largest difference was 3 hours.

<u>TMS, EMG and motion capture</u>

EMG signals were recorded with a standard tendon-belly montage (Ag/AgCl electrodes), on four right intrinsic and extrinsic hand muscles: First Dorsal Interosseus (FDI), Abductor Digiti Minimi (ADM), arm Flexor Digitorum Superficialis (FLX), Extensor Digitorum (EDC). Data was amplified via a wireless electromyography system (ZeroWire EMG, Aurion, Italy), with a band pass between 10-1000Hz. Analog to digital conversion was done via a dedicated board (Power1401 CED, Cambridge Electronic Design Limited, Cambridge, England) at a sampling rate of 2kHz. Right arm TMS-evoked movements were measured via a passive motion capture system (VICON, Oxford, UK) with 9 near infrared cameras with an acquisition frequency of 100Hz. Nine reflective markers were attached on the right hand. Markers were respectively on the nail of the thumb, nail of the index, nail of the middle finger, nail of the ring finger, nail of the 5th finger, ulnar styloid, radial styloid (thumb knuckle), index knuckle, 5th finger knuckle (Figure 1C). TMS was applied using a Magstim 200 stimulator (Magstim Company, Whitland, UK) and a 70 mm figure of eight coil. Coil position was determined at the beginning of session 1 (day 1) and 2 (day 2$_{pre-cTBS}$) based on standard procedures (Rossini et al. 1994; Rossini et al. 2015) to define the optimal coil location for the muscles of interest. In this case, coil position and orientation was optimized to achieve reliable MEPs on all recorded muscles, at the lowest possible intensity. Resting Motor Threshold (rMT) was determined as the intensity evoking at least 50µV MEPs in all the four recorded muscles, at least 5 times out of 10. At the beginning of session 2, the active motor threshold (aMT) was also determined. The aMT was defined as the minimal TMS intensity evoking, in all muscles, 5 out of 10 MEPs of at least 200µV, during voluntary sub-maximal contraction. Once we determined the optimal coil position, we used a mechanical support to fix the coil position with respect to the head. The head was also constrained

by a chin-rest and an ark-shaped two-points support on the forehead and on the right lateral side of the head. We additionally marked the coil outline on the head of the participant (five small marks where drawn directly on the skin with an ink marker to match coil position and orientation). An experimenter was standing behind the participant for the whole duration of the experiment to control that the coil was not displaced at any time with respect to the optimal location identified. TMS was delivered during an approximately equal amount of muscles contraction (all four muscles; 30% maximal) lasting 2s and followed by 8-12s of rest. Muscle contraction onset was prompted by a tone sound and was monitored on a screen by the experimenter and the subject, via continuous visual feedback. Between session 2 (day $2_{\text{pre-cTBS}}$) and 3 (day $2_{\text{post-cTBS}}$) we applied a cTBS protocol over the left primary motor cortex. The cTBS protocol consists of a series of TMS trains (three pulses at 50 Hz) repeated every 200ms for 40s (total of 600 pulses) and it was applied at an intensity of 80% of the aMT (Huang et al. 2005). During the baseline and the action observation protocol, the intensity of stimulation was set at 120% of the rMT. During baseline trials, TMS was delivered at random intervals (ranging between 8-12s) while subjects were asked to rest and relax. During action observation trials a single TMS pulse was delivered on each trial at one of the two possible time points (60 total trials, with 15 pulses for each combination of the two object types with the two stimulation time points; Figure 1B). The first stimulation time point (t_1) corresponded to maximal arm transport acceleration, 250ms from the start. This time point was chosen to offer very little visual information to disambiguate which object was going to be grasped. As shown in Supplementary Material B (Fig. B.2), at timing t_1 (peak acceleration) few differences were visible in the main parameters of the kinematics of the actor (grip aperture, velocity, acceleration, fingers kinematics). The video-clips used as stimuli were chosen specifically to be as similar as possible in the early phase of reaching. The second stimulation timing (t_2) was delivered at maximal transport velocity, 500ms from the start. At this time point a significant amount of visual information about the observed movement is available and this also corresponds to maximal CSE modulation (Gangitano, Mottaghy, and Pascual-Leone 2001). In total, 30 trials for each of the two timings were recorded (15 per grip type).

Data analysis

Preprocessing. The data collected (EMG, motion capture and behavioral responses) were processed with custom software written in Matlab (Mathworks, Natick, MA). From EMG recordings, we computed peak-to-peak maximal amplitude of each MEP for all four muscles, on a variable-length window, after the TMS pulse. The exact window length was set separately for each subject and muscles by averaging all trials in all conditions. This procedure ensures that the window of peak-to-peak computation is tailored to the specific MEPs morphology (Figure 1C). Motion capture data were

25

first low-pass filtered using a digital fifth-order Butterworth filter at a cutoff frequency of 20Hz. We then computed 8 elevation angles (Figure 1C): (1) from radial styloid to nail of thumb, (2) index knuckle to nail of index, (3) index knuckle to nail of middle, (4) 5th finger knuckle to nail of ring, (5) 5th finger knuckle to nail of 5th finger, (6) ulnar styloid to radial styloid, (7) ulnar styloid to index knuckle, (8) ulnar styloid to 5th finger knuckle. Elevation angles are defined by the angle of each segment with the vertical axis. This measure represents not just the displacement of a unique finger, but rather its movement with respect to the movement of the hand and is comparable to previous investigations using inductive sensors (Gentner and Classen 2006). Elevation angles were then low-pass filtered (Butterworth filter at a cutoff frequency of 20Hz). To account for slight changes in the initial hand position, we normalized elevation angles, at each trial level, by the pre-stimulation mean amplitude (500 ms period before TMS). After this pre-processing, the peak-to-peak amplitude of each angular displacement was used to define MEKs. Outliers' values, exceeding 2 standard deviations (SD) from the average of each subject, were discarded (around 5% of trials). In addition, MEPs and MEKs data exhibiting excessive muscle activity prior to the TMS pulse within each experimental session were removed from further analysis (>3 SD; MEPs: 1% of trials, MEKs: 3% of trials). Finally, MEPs and MEKs individual trials values were normalized on the basis of the average of the baseline$_{pre}$ for each session and each subject separately.

Permutation tests. Permutation test is a class of randomization test, based on the computation of the values of the statistical test after all possible randomization of the labels between the compared datasets. Contrary to parametric statistics, these tests do not depend on priors or on the form of the populations sampled, and showed more reliability in case of violations of these foundational assumptions (Byrne 1993; Hunter and May 2003). Randomization techniques, such as permutations test, are particularly relevant for cognitive/experimental psychology relying on small samples (Byrne 1993; Hunter and May 2003; Killeen 2005), situation in which they outperform the classical parametric approaches (Ludbrook and Dudley 1998; Nichols and Holmes 2001). Thus, permutation test, as a conservative strategy, are becoming the method of reference in EEG, MEG and fMRI studies (Eklund, Nichols, and Knutsson 2016; Maris and Oostenveld 2007; Nichols and Holmes 2001; Pantazis et al. 2005; Singh, Barnes, and Hillebrand 2003). For these reasons, permutation tests are a well-suited tool for the investigation of AOEs via TMS and we present only the statistic values reported by this technique (results from parametric tests can be found in Supplementary Material D). Comparing two datasets A and B with permutation tests, an absence of significant differences suggests that, the labelling of the data under investigation could be considered as arbitrary and that the same data would have arisen whatever the experimental condition is. The method generates shuffled data sets by randomly permuting the labels associated to the conditions and estimating the

sampling distribution of the test statistic under this strong null hypothesis. Repeating the process many times, a distribution of test statistics is obtained representing the distribution under the null hypothesis. Then, the null hypothesis is rejected at a significance level if the tested statistic is greater than the $1-\alpha$ percentile of the empirical permutation distribution (where α is the significance level). At the end, the final p-value gives the proportion of occasions on which the data would have segregated into such disparate groups by chance. We performed multiple permutation tests using the matlab function 'mult_comp_perm' using 5000 repetitions. When applying permutation tests with multiple comparisons a correction must be performed. The "tmax" method was used for adjusting the p-values of each variable in the same way as Bonferroni correction does for a t-test (Blair and Karniski 1993; Westfall and Young 1993).

Statistical analysis. We performed four different groups of multiple comparisons using two-tailed corrected permutation test on all variables (4 MEPs and 8 MEKs). (1) <u>Generic attentional effects</u>: the first analysis was aimed at evaluating non-specific action observation or attentional effects. Specifically, we analysed the temporal evolution of our dependent variables where no AOEs are expected (baseline$_{pre}$ trials vs. baseline$_{post}$ vs. AO trials with stimulation at t_1 in both grasp-type conditions ($t_{1power\&precision}$)). All possible comparisons between these 3 conditions were run for session 1 and 2 separately (day 1 and day 2$_{pre-cTBS}$). (2) <u>Action observation effects</u>: the second analysis was directed to the investigation of AOEs. For this purpose, we ran multiple permutation tests to compare the grasp-type conditions (precision and power) and the two timings (t_1 vs. t_2). For each pre-cTBS session separately (day 1 and day 2$_{pre-cTBS}$), all possible comparisons between these 4 conditions were performed. (3) <u>Effects of cTBS on M1</u>: the third analysis was performed to evaluate the effect of cTBS on baseline trials (pre-post cTBS effects on all MEPs and MEKs). Since the effect of cTBS has been reported to be highly variable across participants (Huang et al. 2005; Palmer et al. 2016; Ridding and Ziemann 2010; Vallence et al. 2015; Vernet et al. 2014; Hamada et al. 2013), we also show the effect of cTBS, on corticospinal excitability, at the single subject level as a separate piece of information (see Figure A.1 in Supplementary Material A). At the group level, we ran a simple two-tailed permutation test on each variable. At the subject level, we ran a series of paired two-tailed t-tests, between the measures recorded at rest before the cTBS protocol (baseline$_{post}$ – day 2$_{pre-cTBS}$) and the ones recorded at rest 5 minutes after (baseline$_{pre}$ day 2$_{post-cTBS}$). (4) <u>Effect of cTBS on AOEs</u>: the last analysis was performed to evaluate the change in the AOEs following cTBS application. We ran multiple permutation tests to compare the grasp-type conditions (precision and power) on timing t_2, between the two sessions (day$_{2\ pre-cTBS}$, day$_{2\ post-cTBS}$). All possible comparisons between these 4 conditions were performed. This analysis was repeating two times: (1) in normalizing by the baseline$_{pre}$ of each session, (2) in normalizing by the baseline$_{pre}$ of the session 2 (day$_{2\ pre-cTBS}$).

Principal Component Analysis. A Principal Component Analysis was used to investigate the modulation in the whole hand pattern of movement elicited by TMS. This method is classically used as an index of movement coordination evaluation (Paizis et al. 2008; Berret et al. 2009; Daffertshofer et al. 2004; Hicheur, Terekhov, and Berthoz 2007) and has already been employed in previous investigations on TMS-evoked movements (Gentner and Classen 2006). This procedure uses an orthogonal transformation to convert selected variables into a set of new variables, less numerous, linearly uncorrelated and named principal components. These new variables are the results of linear combination of the initial variables explaining the maximal variance of the dataset. This operation can be thought as an efficient manner to reveal the hidden internal structure of a multivariate dataset in a way that best explains the variance in the data. As done by (Gentner and Classen 2006), we defined for each trial a posture vector formed by the value of the eight elevation angles at a precise time-point. This time-point was computed as the time where the absolute sum of joint angles (relative to baseline) reached a maximum in the temporal window from 0 to 150ms after the TMS pulse. Separate PCAs were performed for each participant and for each condition on a matrix M, composed of m=30 rows (number of trials for each grasp type) and n=8 columns (number of angles). Each column $M_{i \ (1 \leq i \leq n)}$ of M was centered and normalized. Based on this transformation, the covariance matrix of M was computed and orthonormally diagonalized to obtain the matrix of the eigenvectors. Eigenvectors were then reordered in a decreasing order based on the value of the associated eigenvalue. This new matrix, denoted W (formed by the columns $(w_{ij})_{i \leq 1, j \leq 1}$) contained the weighting coefficients or loadings associated to the principal components. Then, the principal components (denoted by PC), are defined by the following linear combination: PC = MW. Deduced from this, the first PC is obtained by the following equation:

$$PC_1 = \sum_{i=1}^{8} w_{i,1} M_i$$

The first eigenvector (associated to the first principal component) represents the direction of the maximum variance. The ratio between the first eigenvalue and all the eigenvalues gives a number between 0 and 1 (converted in percentage and reported as PC%). Expressed at each subject level, variance explained by the first PC captures the amount of "invariance" between movements across trials. Functionally speaking, a high PC% value means that markers movement are dependent and suggest a grouped control of the variables instead of an individual control of each joint.

From this computation, we analysed across subjects the number of components necessary to obtain a PC%≥90, and the PC% value for a number of 3 and 4 components (average number of components found across subjects). We first ran multiple permutation tests defined similarly to the three analyses

performed on MEPs and MEKs (see *2.5.3 Statistical Analysis*: <u>Generic attentional effects</u>, <u>Action Observation Effects</u> and <u>Effects of cTBS over M1</u>). These computations showed no significant effect and interaction for any variable. However, since PCA analysis requires a large amount of data (Gentner and Classen 2006), this absence of significance was expected. We then performed a second analysis by grouping together trials belonging to the two grasp types (precision and power) in order to increase the number of observations. Multiple one-tailed permutation tests were then run to compare baseline vs AO trials (baseline, t_1, t_2) within and between all sessions (day1, day2$_{pre-cTBS}$, day2$_{post-cTBS}$).

(c)   Results

In the following section, we present the modulations observed on the MEPs for the 4 recorded muscles (FDI, ADM, FLX, EDC) and on the MEKs for the 8 elevation angles (thumb, index, middle, ring, 5th finger, thumb knuckle, index knuckle, and 5th finger knuckle), in function of the different experimental conditions: timing of TMS pulse (t_1, t_2), observed grip type (power, precision) and sessions (day 1, day 2$_{pre-cTBS}$, day 2$_{post-cTBS}$).

We will first present the generic modulation induced by the observation of an action. In a second part, we will investigate the specific modulation of MEPs and MEKs related to grip type (power vs precision) before cTBS application (day 1 and day 2$_{pre-cTBS}$). Then we will describe the effect of cTBS (day 2$_{post-cTBS}$) on the previously observed modulations. To finish we will analyse modularity of TMS-evoked movements, by applying PCA data reduction to the MEKs data, to explore how these coordination patterns are affected by action observation and cTBS application. For graphical reasons, we present in this section only the principal actors of the movement. The additional variables modulations are shown in Supplementary Material C.

<u>Generic attentional effects</u>

These analyses focused on changes of MEPs and MEKs measures that cannot be attributed to specific AOEs (i.e. differences in the observed grasping movements), but rather to a generic modulation related to action observation or attentional effects. The permutation test highlighted a generic action observation effect in the first and second session (day 1 and day 2$_{pre-cTBS}$) on the MEPs from all 4 muscles, by showing an increase of the MEPs recorded at timing $t_{1\ precision\&power}$ with respect to baseline$_{pre}$ ($p<0.05$; Figure 2). On the MEKs, this effect appeared on the index in the day 2$_{pre-cTBS}$ only ($p=0.013$; Figure 2). In addition, an increase from baseline$_{pre}$ to baseline$_{post}$ appeared for FDI ($p=0.007$) and FLX ($p=0.001$) on day 2$_{pre-cTBS}$. Altogether, MEPs measures displayed stronger generic attentional-related effects with respect to MEKs measures.
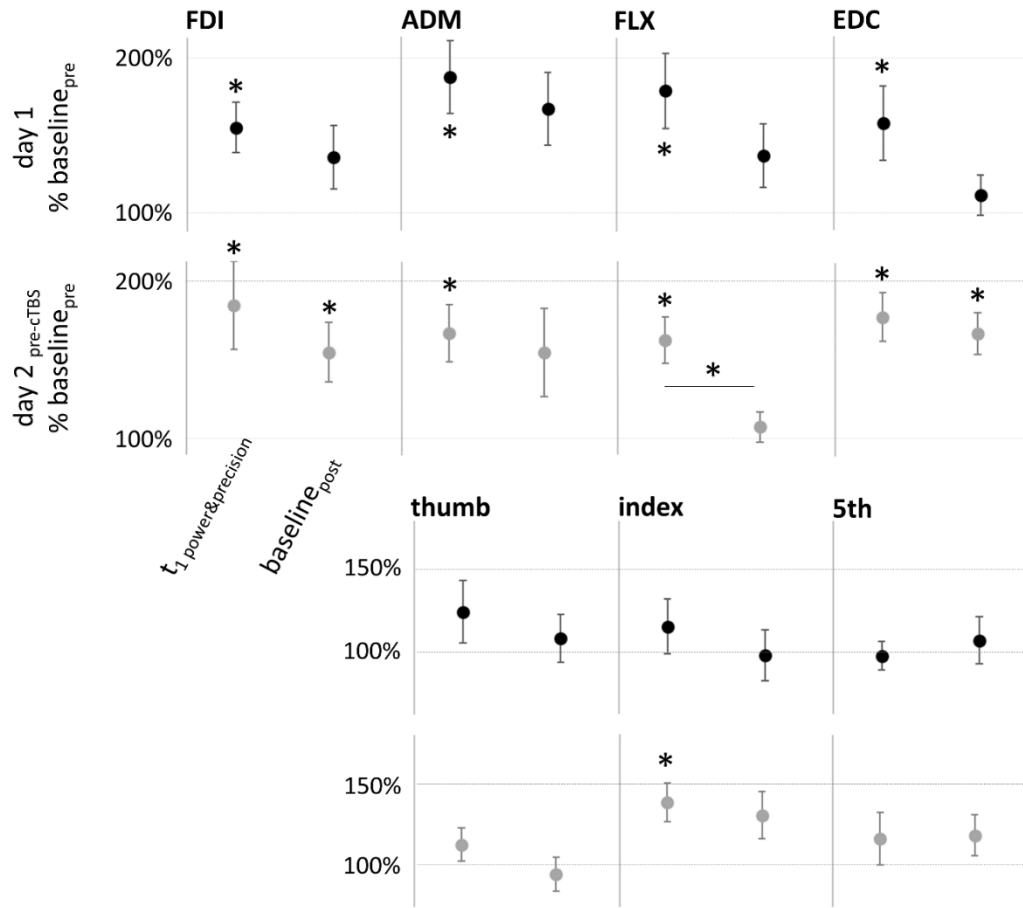
Figure 2: Generic attentional effects on MEPs and MEKs amplitude.
Mean and standard error for the four muscles (FDI, ADM, FLX, and EDC) MEPs and three elevation angles MEKs (thumb, index and 5th) are shown as a percentage (%) of the average of baseline$_{pre}$ on the y-axis. The two sessions are stacked vertically for each measure (day 1 on top, day 2$_{pre-cTBS}$ on bottom). The baseline$_{pre}$ level is represented by the low horizontal bar (100%). The 2 phases contrasted (timing 1$_{power\&precision}$, baseline$_{post}$) are shown on the x-axis. Significant differences (p<0.05) with baseline$_{pre}$ are represented by an asterisk in the top of the value, between the two phases by a horizontal segment surmounted by an asterisk. The Y-axis scale is the same within variables (MEPs [90 to 210%], MEKs [60 to 180%]). X-axis labels are constant across variables and are reported on for the first variable (FDI).

Action observation effects

These analyses focused on contrasting the specific modulations induced by the observation of the two grasping actions (i.e., the classical AOEs). The permutation test highlighted a grasp-type related modulation at timing t2 (i.e. mirror-like effect; Figure 3) on EDC MEPs (day 2$_{pre-cTBS}$: p=0.028) and thumb MEKs (day 1: p=0.043; day 2$_{pre-cTBS}$: p=0.014). Therefore, the thumb MEKs tracked the expected AOEs reliably across sessions, whereas the MEPs result was not present in the first session. In addition, the contrast between the two timings revealed an increase from t$_{2\ power}$ to t$_{1\ power}$ (p=0.028)

and $t_{1\ precision}$ (p=0.048) on day$_{2\ pre-cTBS}$, and of the index MEKs (precision, day 1: p=0.001) at timing t_1 with respect to timing t_2 (Figure 3).
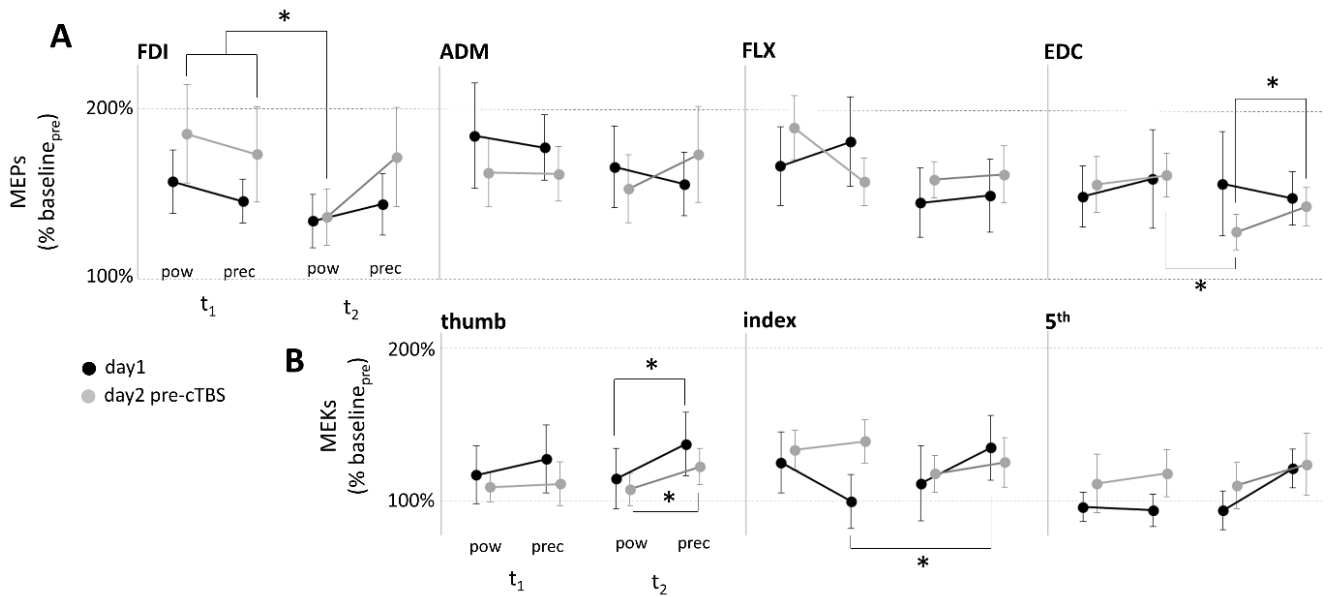
Figure 3: Action observation effects on MEPs and MEKs amplitude.
Mean and standard error of the four muscles (FDI, ADM, FLX, and EDC; panel A) and MEKs (thumb, index and 5th; panel B) expressed as a % of the average of baseline$_{pre}$, separately for session (day 1, day 2 $_{pre-cTBS}$), timing (t_1, t_2), and grasp type (precision (prec), power (pow)). Significant differences are represented by an asterisk (p<0.05). X-axis labels are constant across variables (referred to the first panels 'FDI' and 'thumb').

Effect of cTBS over M1

This analysis aimed at verifying the general efficacy of the cTBS protocol in inhibiting TMS-evoked responses at rest (baseline$_{pre}$ and baseline$_{post}$). On average, cTBS reduced the baseline MEPs amplitude of 19% for FDI, 32% for ADM and FLX, and 28% for EDC (Figure 4). Permutation tests showed a significant effect on FLX (p=0.008) and EDC (p=0.035) (Figure 4). On MEKs, an increase of amplitude following cTBS was observed for the thumb (37%), index (10%), and thumb knuckle (15%) while a decrease was found for the middle (19%) and 5th finger (20%). No change (<5%) was noticed for ring, index knuckle and 5th finger knuckle (Figure 4). None of these MEKs modulation are significant after permutation tests. In addition, the effect of cTBS at the subject level, on EDC MEPs and thumb MEKs can be found in Supplementary Material A (Figure A.1).
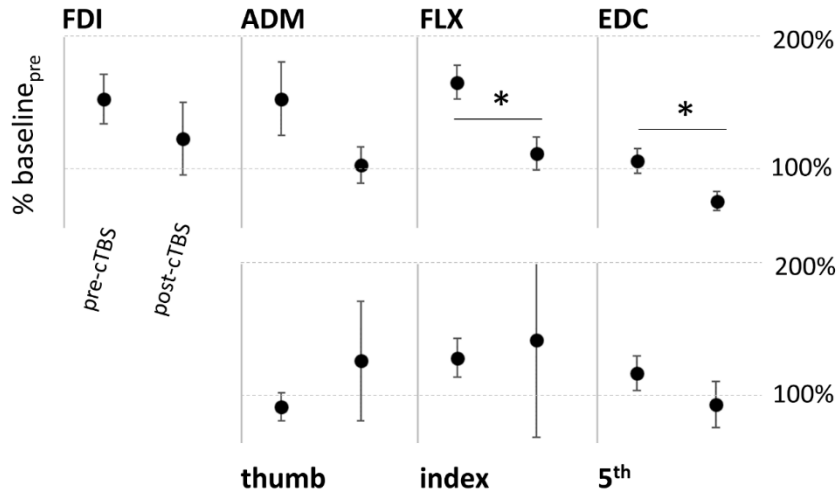
Figure 4: Effects of cTBS on baseline MEPs and MEKs.

For each graph, the first point (to the left) represents the mean and standard error of the 15 baseline trials recorded before cTBS (pre-cTBS). The second point (to the right) represents the mean and standard error of the 15 baseline trials recorded after cTBS (post-cTBS). Asterisks denote significant differences (p<0.05). X axis labels are constant across variables (referred to the first panel 'FDI').

Effect of cTBS on AOEs

This analysis focused on the inhibitory effect that a cTBS stimulation over the primary motor cortex has on both MEPs and MEKs AOEs, by examining the AOEs after the cTBS protocol (day $2_{\text{post-cTBS}}$). On day $2_{\text{post-cTBS}}$, no significant AOEs modulations (precision vs power and t_1 vs. t_2) were found for MEPs and MEKs (p>0.05; Figure 5). As shown in 3.2, a significant AOEs modulation was found only for thumb MEK (p=0.007) and EDC MEP (p=0.023). The exact same significant modulations were found for the two types of normalization. These results show that the cTBS protocol affected the previously reported AOEs on both the MEPs and MEKs.
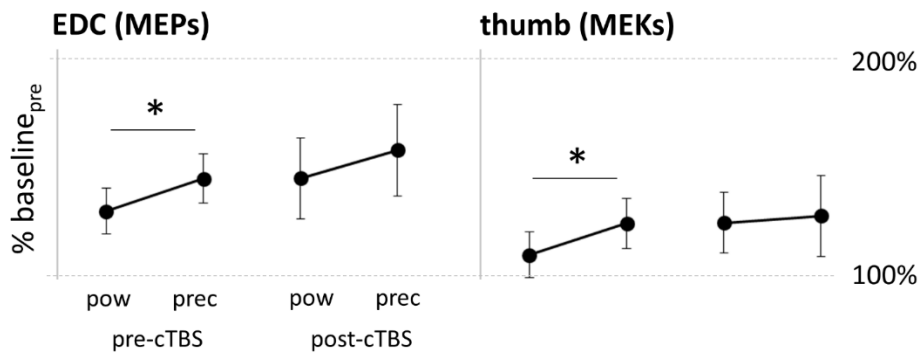
Figure 5: Effects of cTBS on AOEs.

Mean and standard error of EDC MEP (A) and thumb MEK (B), as a function of grasp type (precision (prec), power (pow)) at timing t2, before (left side) and after (right side) cTBS protocol over M1. All values are expressed as a % of the average of baseline$_{pre}$ for each session. Asterisks denote significant differences (p<0.05). X axis labels are constant across variables (referred to the first panel 'EDC').

Movement modularity evaluation

The PCA analyses were employed to investigate if the whole hand pattern of movement coordination elicited by TMS was altered by action observation and by cTBS over the primary motor cortex. On average, the first four PCs accounted for 93%, 93.1%, 92.5% of the variance in day1, day2$_{pre-cTBS}$ and day2$_{post-cTBS}$ respectively, with the first two accounting for 74.1%, 74.7%, 73.9% of the variance. This result is in agreement with previous reports showing, with a larger amount of data, that the first four PCs accounted for 89.3% of the variance, with the first two accounting for 72.6% (Gentner & Classen, 2006). Furthermore, we intended to measure if cTBS altered the AOEs and baselines. We ran the permutation tests to contrast baseline vs AO trials (baseline$_{pre\&post}$, t1$_{power\&precision}$, t2$_{power\&precision}$) within and between sessions (day 1, day 2$_{pre-cTBS}$, day 2$_{post-cTBS}$). A significant PC% reduction of baseline day 2$_{post-cTBS}$ compared to baseline in day 1 (p=0.015) and day2$_{pre-cTBS}$ (p=0.049) was revealed (Figure 6). Moreover, a significant PC% increase at t2$_{power\&precision}$ compared to baseline was found on day 2$_{post-cTBS}$ (p=0.029). These results suggest that the cTBS affected the organization of coordinated hand movements at baseline, while the action observation partially restored it.
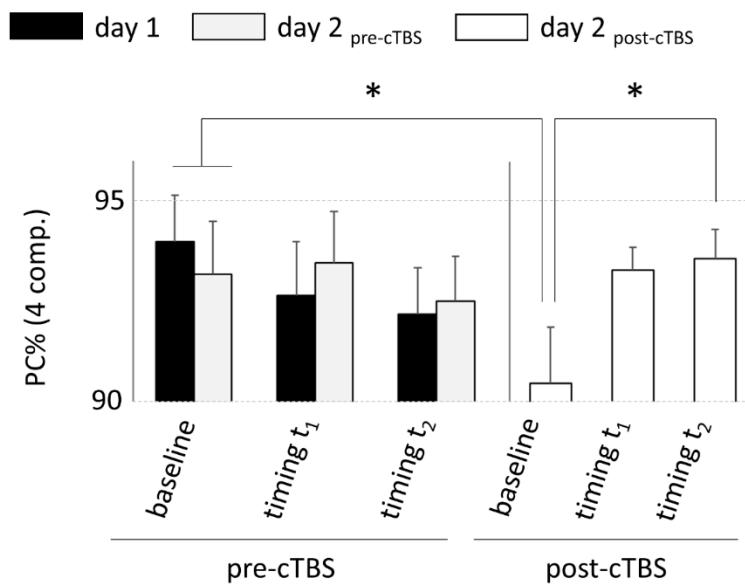
Figure 6: Whole hand configuration changes across sessions and conditions.
PC% values of the fourth first components (y-axis), computed on the 8 elevation angles, are shown for baseline and AO trials (baseline, timing t₁ and timing t₂) for the three sessions (day 1, day 2$_{pre-cTBS}$, day 2$_{post-cTBS}$). Asterisks denote significant differences (p<0.05).

(d)   Discussion

The present study evaluated, side-by-side, motor evoked potential (MEPs) and TMS-evoked kinematics parameters (MEKs) to characterize action observation effects in humans. The experimental protocol consisted in a classical action observation task (i.e. Gangitano et al., 2001),

involving reaching-grasping towards either one of two objects with different sizes (thus affording power or precision grip). MEPs amplitude during all action observation conditions increased with respect to baseline. This increase is associated to generic action observation because it is not action-specific (i.e. precision vs. power grasping; Fadiga et al., 1995; Strafella and Paus, 2000; Aziz-Zadeh et al., 2002; Clark et al., 2004). Therefore, it cannot be excluded that in our experiments MEPs modulation is driven by a more general attentional grab due to the increased saliency of moving visual stimuli. On the contrary, this effect did not appear on MEKs, suggesting that these measurements are less prone to attentional modulations.

The critical modulation that we were expecting was related to the grip type (precision vs. power grip) particularly at the later stimulation timing (t_2, as opposed to the earlier timing t_1, when far less action-specific visual cues are available). As we found in our data, larger responses for precision grip were more likely to occur at t_2. Precision grip requires indeed more accuracy in finger positioning and consequently greater control on muscle activity during execution (Marzke 1997; Gribble 2003). Moreover, as shown by cortical stimulation and recording experiments performed on monkeys (Fluet, Baumann, and Scherberger 2010; Rizzolatti et al. 1988) and humans (Pistohl et al. 2012), precision grip has a larger cortical representation than power grip.

Our results showed a clear difference between the two kind of measures. While MEPs at t_2 increased only for finger extensors and only in one session, a significant MEKs modulation at t_2 was found for the thumb elevation angle in both recording sessions. This major involvement of the thumb could be related to its fundamental role in grasping tasks (Cotugno, Althoefer, and Nanayakkara 2016) and to the larger probability in evoking thumb movements via TMS stimulation (Gentner and Classen 2006). For both measures (extensor muscle MEPs, thumb MEKs), after the application of cTBS over M1 significant AOEs modulation was not observed anymore. This result do not match with previous reports showing no change in CSE-based AOEs (Avenanti et al. 2007) or in behavioral execution-adaptation effects (Cattaneo and Barchiesi 2011), after the application of cTBS over M1. While contrasting with previous findings, our results are in line with the recent demonstration that M1 cTBS alters behavioral performance in an action observation task (Palmer et al. 2016). Further studies will be necessary to fully understand the role played by M1 in AOEs, especially in light of the discovery that in non-human primates, neurons with mirror-like properties have also been found in the primary motor cortex (Tkach, Reimer, and Hatsopoulos 2007; Dushanova and Donoghue 2010; Kraskov et al. 2014).

Although the use of MEKs requires a greater amount of data processing and the selection of the kinematic parameters of interest (i.e., elevation angles in the present work; Gentner and Classen, 2006), we demonstrated that the use of TMS-evoked thumb kinematics provides a greater

reproducibility of AOEs. Importantly, we evaluate AOEs via statistical methods that, by incorporating biophysically motivated constraints in the test statistic, drastically increase sensitivity of the statistical test (Maris and Oostenveld 2007). Strikingly, the recording of MEPs alone did not show the emergence of consistent AOEs (Fadiga et al. 1995; Fadiga, Craighero, and Olivier 2005; Naish et al. 2014). Although reproducibility issues are becoming more and more important (Kobayashi and Pascual-Leone 2003; Mills 1999), this is rarely verified. Our findings, together with the known difficulty in publishing negative results (Matosin et al. 2014; Mervis 2014), suggest that a quite significant number of unpublished studies did not find AOEs using classical CSE measures (i.e. MEPs). Although a larger number of subjects or trials might have shown effects on MEPs in both sessions, the critical point here is that another measure recorded in parallel (MEKs) can show the same AOEs twice, with the same number of trials and subjects. As a consequence, it is here more interesting to discuss why MEKs should be more consistent than MEPs.

To understand why MEPs could be more affected by confounds it is important to consider some key experimental constraints. In action observation studies, the classical procedure consists in focusing on very few muscles (up to two or three) and stimulation is applied just above threshold to maximize response sensitivity to AOEs modulations. Recording MEPs on several muscles would require higher TMS intensities, to accommodate for the different thresholds and partially non-overlapping representations. Increasing stimulation intensities though, would sample from different regions of the recruitment curve in each individual muscle (Devanne, Lavoie, and Capaday 1997), and this is known to affect MEPs sensitivity to AOEs (Loporto et al. 2013). Therefore, recording from very few muscles is primarily driven by technical limitations in measuring reliable CSE. This is a potential reason for which we do not find a clear replicable modulation on the MEPs, while we do on the MEKs.

Although the solution may seem to record less muscles, this is a sub-optimal choice to explore AOEs for goal-directed actions. In fact, in a realistic scenario (e.g. movement execution to reach an object), small postural changes (such as those caused by a change in height of the table) have a dramatic influence on the temporal evolution and recruitment of the same muscle in the same action towards the same goal. The same amount of EMG activity in one muscle is present in many different actions and is not necessarily predictive of the action goal. For example, finger extensors activation while lifting an object is in principle against the goal of applying forces onto an object, but it is necessary, via co-contraction with the flexors, to stabilize fingers and wrist joints. Therefore, recording from finger extensor only, would not allow us to discriminate the act of opening or closing fingers. In general, during action execution, little discriminative information can be extracted from the activity of one (or few) muscle(s)).

Many AOE studies instead, used intransitive (non goal-directed) simpler movements, involving few muscles, such as the abduction-adduction of the index or the 5th finger (Maeda, Kleiner-Fisman, and Pascual-Leone 2002; Urgesi et al. 2006; Catmur, Walsh, and Heyes 2007). This situation offers a direct one-to-one mapping between cortical recruitment, muscle activities and observed movement kinematics. At the same time, these experimental settings may offer a limited insight about the neural mechanisms at play during naturalistic action observation. Nevertheless, these simplified action observation protocols were used to debate about the origin of mirror-like activities in general (Cook et al. 2014). Specifically, if AOEs are the by-product of sensorimotor associative learning or do they represent a genetic adaptation to fulfil a specific socio-cognitive function? (Catmur, Walsh, and Heyes 2007; Barchiesi and Cattaneo 2013; Cavallo et al. 2014).

We concur that understanding the relationship between AOEs and the plastic modulations induced by action observation learning is important. In fact, typical AOEs studies propose long sessions of repetitive action observations, which is the exact same protocol used to induce observational learning effects (Celnik et al. 2006; Williams and Gribble 2012; Stefan et al. 2005; Stefan et al. 2008), thus creating a fundamental confound between these two components. Here we show a baseline increase from pre to post-action observation on the MEPs (see "3.1 Generic attentional effects"). Crucially, this effect never appeared on MEKs, indicating greater independence from these learning-induced changes. The reason could be that MEKs convey a richer description of the multidimensional nature of the descending volley. In fact, whole-hand TMS-evoked motor synergies more than muscle-level modulations, have been shown to be relatively robust to long term motor learning (Gentner et al. 2010). It remains to be seen whether MEKs during goal-directed action observation are affected by short-term counter-mirror observational training, as it was the case for CSE in simple intransitive movement observation (Catmur, Walsh, and Heyes 2007).

More importantly from a theoretical point of view, similar kinematic patterns (and thus visual appearance) may very well be associated to quite different muscle recruitment over time and space. Redundancy and invariance principles in action execution (Guigon, Baraduc, and Desmurget 2007; Sporns and Edelman 1993; Flash and Hochner 2005), suggest that the functional kinematic output, more than the activities of (few) muscles, provides the best action goal description. These considerations are based on behavioral observations of how kinematics relates to (multi-) muscle activity. At the same time, if we look at the anatomical targets of the descending corticospinal tract, its role and function becomes clearer. In fact, direct corticospinal projections largely target the dorsal horns at the spinal level, meaning that muscle activity is mediated by divergent interneuronal connectivity (Jankowska 1992; Nielsen 2016). Projections to the ventral horn, which are a relatively new product of evolution, instead target different spinal motor nuclei, innervating different muscles

at the same time (Fetz and Cheney 1980; Porter and Lemon 1993). It is for these reasons why MEKs may be better suited to measure goal-directed AOEs. MEKs measure the effect of the synergistic activity of multiple muscles producing coordinated movements, which are driven by intracortical, corticospinal, spinal and peripheral influences.

When we move to the level of whole-hand coordination, we know it is neither based on muscle by muscle nor on single finger movement control. In fact, hand control relies on the temporo-spatial grouping of muscle activities that is further constrained by joint movement biomechanics. Thus, to consider the organization of the motor system, AOEs should be evaluated even beyond separated joint movements. To do so we performed a PCA on the TMS-evoked posture vectors composed by all joints movements. As previously found, a small set of three to four PCs accounted for much of the data variance of TMS-evoked movements (Gentner and Classen 2006). Whole-hand coordination, however, did not show any modulation for grip type observation. This can be explained by the relatively small amount of data-points we could use to extract uncorrelated whole-hand synergies (i.e. PCs). Previous investigations have indeed shown that at rest, single pulse TMS evoked a quite large number of different postures (Gentner and Classen, 2006). Despite this, we found a significant modulation of whole-hand coordination following cTBS application. Our data revealed a global disturbance of whole-hand coordination due to cTBS-driven injection of noise in the organization of hand movements (Miniussi, Harris, and Ruzzoli 2013). The same analyses revealed also a significant increase in coordination between action observation (at timing t_2) and baseline recordings after the application of cTBS. This finding suggests that action observation partly countered the interfering effect of cTBS over primary motor cortex.

In conclusion, we showed in this study that MEKs act as a more effective measure than MEPs in describing the motor activities triggered by action observation. Specifically, MEKs seem to be more robust to the two critical confounds that can occur when investigating AOEs: observational learning and attentional modulations. These differences are in agreement with other studies showing that while MEKs discriminate between observed actions with different effectors, while MEPs did not (Finisguerra et al. 2015). This lack of sensitivity could ultimately derive from the small amount of information we can extract from MEPs recorded from one muscle. Neural control of arm and hand movements is the consequence of many adjustments at the muscular level (Bernstein 1967; Bizzi et al. 1984; Gribble 2003), following possibly a synergistic organization (D'Avella et al. 2006; Gentner and Classen 2006; Santello, Baud-Bovy, and Jörntell 2013; Leo et al. 2016). In the present study, we demonstrate that recording the net motor output is substantially less ambiguous and more robust in describing the nature of AOEs. The shift from a single muscle to a functional output perspective frames the investigation of AOEs within current models of action control.

(e)   Additional data and analyses

A: Study 1.1: Evaluation of cTBS effects at the single subject level
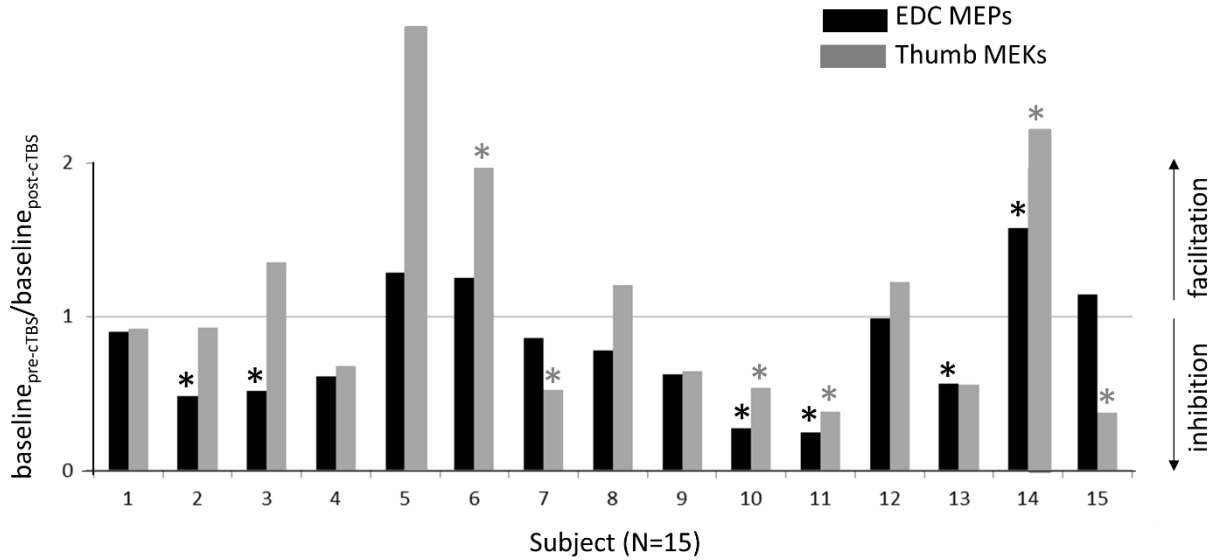
Figure A: Evaluation of cTBS effects at the single subject level.
Bars represent, for each subject, the ratio between the average of the 15 baseline_{post} for EDC MEPS (light grey) and thumb MEKs (dark grey) in session 2 (baseline_{pre-cTBS}) with the 15 baseline_{pre} recorded in session 3 (baseline_{post-cTBS}). Values smaller than 1 indicate a reduction of amplitude in post-cTBS baseline recordings, indexing the expected inhibitory effect of cTBS on each measure. Asterisks denote a subject-wise significant cTBS effect (t-test; p<0.05). Large Inter-subject variability of cTBS effects is also supported by studies and reviews (Ridding and Ziemann 2010; Vernet et al. 2014; Vallence et al. 2015)

B: Study 1.1: Stimuli kinematic and muscular description

In order to choose the most relevant stimuli, we recorded 40 repetitions of an actor performing reach-to-grasp movements toward the two objects (small and large sphere, 20 movements each, Figure 1B of the main text). We selected one movie per grip type (power and precision) based on duration, wrist velocity, wrist acceleration and grip aperture. The following section shows a detailed description (EMG and kinematic) of the 40 repetitions of the movements and of the two stimuli selected.

Kinematic: By analyzing the trajectories for the two movements selected as stimuli in the present work, it is possible to notice that the thumb elevation angle increased more in precision grip than power grip, and that this change appeared late relatively to timing 2. The precision grip movement was associated to a smaller displacement of the index at both timing 1 and 2. The index knuckle, reflecting wrist movement, was unchanged in function of grip type (Figure A.2).
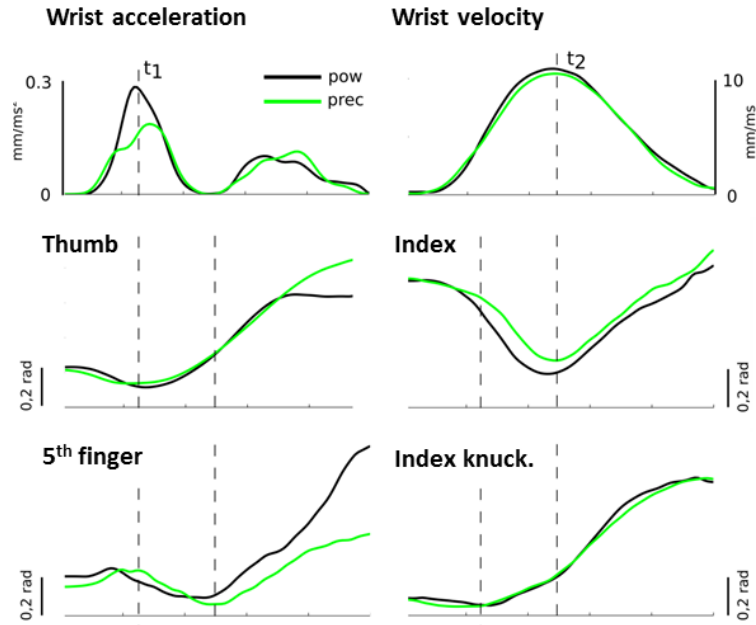
Figure B1: Stimuli kinematic features.
Wrist velocity and acceleration and angular trajectories of thumb, index, 5ᵗʰ finger and index knuckle recorded during the execution of the two movements selected as stimuli, showing the power grasp (pow) in black and precision (prec) in green. The two vertical dashed lines denote the two time-points (t_1 and t_2) selected to deliver the single-pulse TMS during the action observation part of the experiment.

By analyzing the average across the 20 repetitions of the two movements (power and precision), the kinematic parameters did not show any clear modulation related to grip type around timing t_1 and t_2 (Figure A.3). It is important to note that one marker (thumb knuckle) was missing in the actor kinematic as compared to the MEKs recording. To compute the thumb elevation angle we then used the segment from the thumb apex to index knuckle (Figure A.2 and A.3). This change in computation could influence the trajectory showed here.
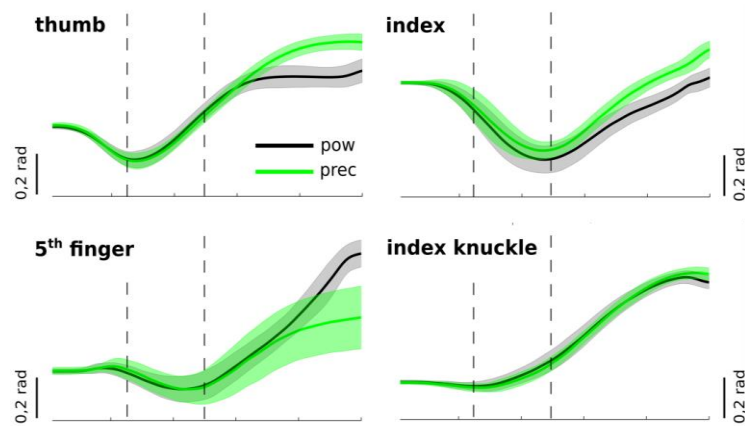
Figure B2: Movement repetitions kinematic features.
Mean and standard deviation of four elevation angles trajectories (thumb, index, 5ᵗʰ finger, index knuckle), for the 40 repetitions of the reaching movements recorded (20 precision grip, 20 power

grip). The power grasp is plotted in black and precision in green. The two vertical dashed lines denote the two timings (t_1 and t_2) selected to deliver the single-pulse TMS during the action observation part of the experiment.

EMG: By analyzing the EMG data from the 20 repetitions of the two movements, EDC and FLX muscles revealed no clear grip-type-modulation. FDI and ADM muscles showed a difference around timing t2: a greater and earlier increase in amplitude when performing a reach-grasp movement aiming at a precision grip compare to power grip (Figure A.4A).

By analyzing the EMG activity recorded during the execution of the two movements selected as stimuli in the present work, we showed that FDI activation amplitude changes depending on the grip type. This difference was in the opposite direction as compared to the data from the 40 repetitions, being increased for power grip with respect to precision grip around timing 2 (Figure A.4B). The data recorded from FLX and ADM also showed a modulation, with greater activity for the movement aimed at the power grip around timing 1.
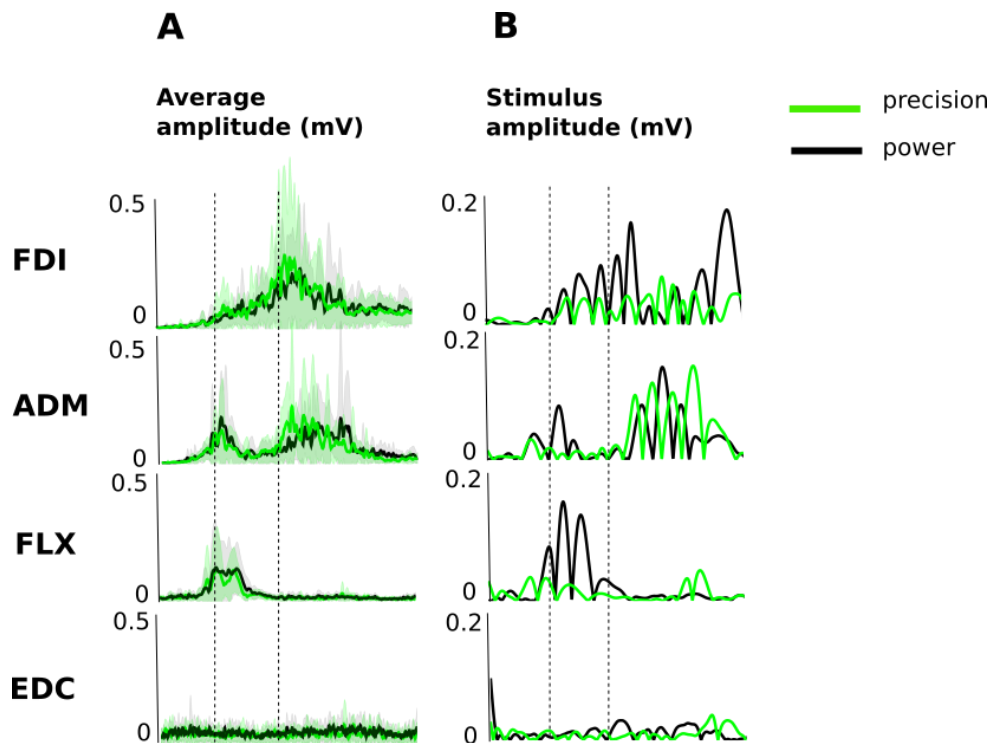
Figure B3: Stimuli and movement repetitions EMG recordings
A. Movement repetitions EMG recordings. Mean and standard deviation of activation of the four muscles (FDI, ADM, FLX, EDC) calculated across the 40 repetitions of the reaching movements recorded on the actor (20 precision grip, 20 power grip). B. Stimuli EMG recordings. Muscular activation for the four muscles (FDI, ADM, FLX, EDC) in the two movements selected as stimuli. For both panels, power grasp is plotted in black and precision in green, and the two vertical dashed lines denote the two timings (t_1 and t_2) selected to deliver the single-pulse TMS during the action observation part of the experiment.
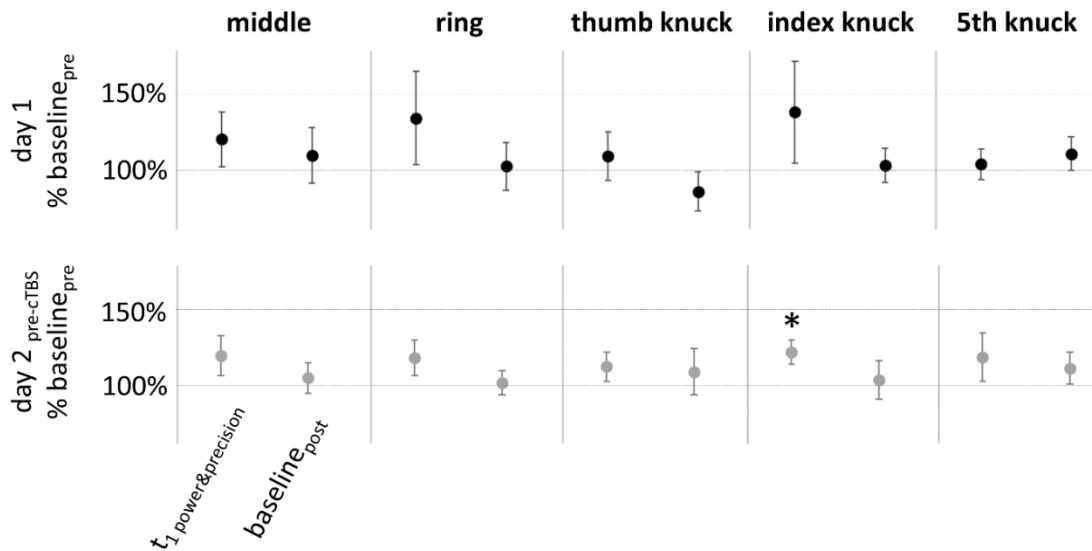
Figure C1: Generic attentional effects on MEKs amplitude.
Mean and standard error for the five elevation angles MEKs (middle, ring, thumb knuckle, index knuckle and 5th knuckle) are shown as a percentage (%) of the average of baseline$_{pre}$ on the y-axis. The two sessions are stacked vertically for each measure (day1 on top, day2$_{pre-cTBS}$ on bottom). The baseline$_{pre}$ level is represented by the low horizontal bar (100%). The 2 phases contrasted (timing $_{1power\&precision}$, baseline$_{post}$) are shown on the x-axis. Significant differences (p<0.05) with baseline$_{pre}$ are represented by an asterisk in the top of the value
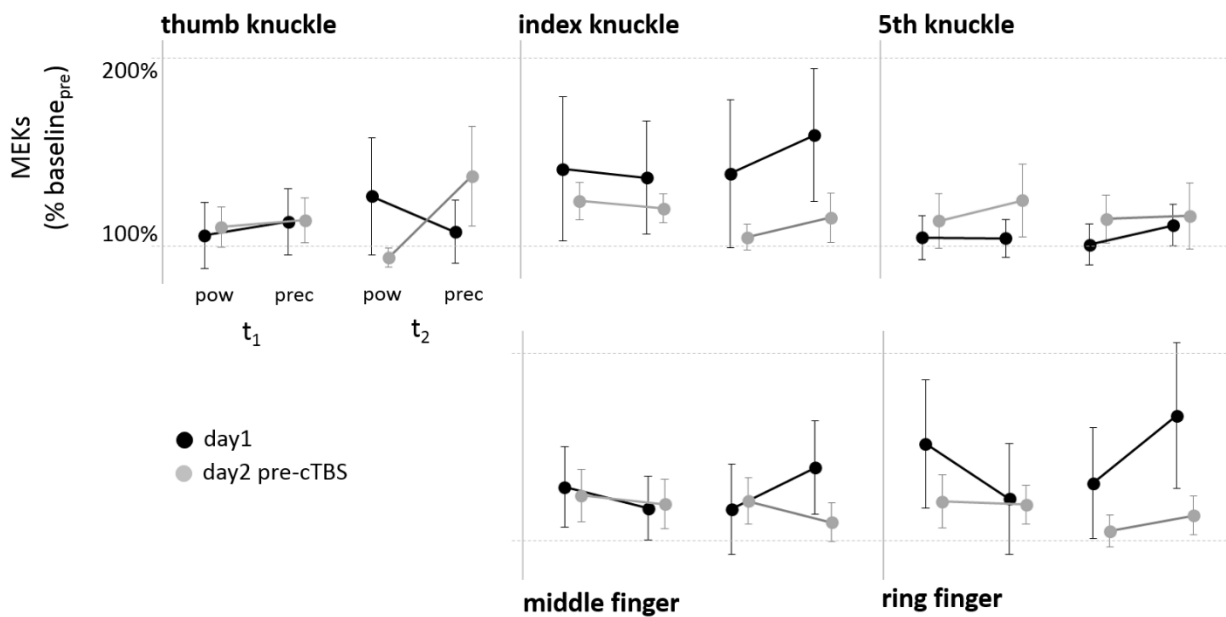
Figure C2: Action observation effects on MEKs amplitude.
Mean and standard error of the five MEKs (middle, ring, thumb knuckle, index knuckle and 5th knuckle) expressed as a % of the average of baseline$_{pre}$, separately for session (day1, day2pre-cTBS), timing (t1, t2), and grasp type (precision (prec), power (pow)).
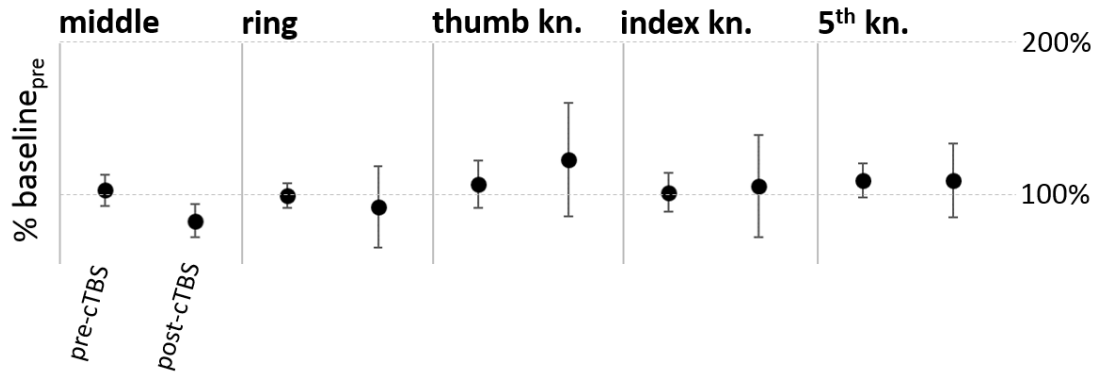
Figure C3: Effects of cTBS on baseline MEKs.

For each graph, the first point (to the left) represents the mean and standard error of the 15 baseline trials recorded before cTBS (pre-cTBS). The second point (to the right) represents the mean and standard error of the 15 baseline trials recorded after cTBS (post-cTBS).
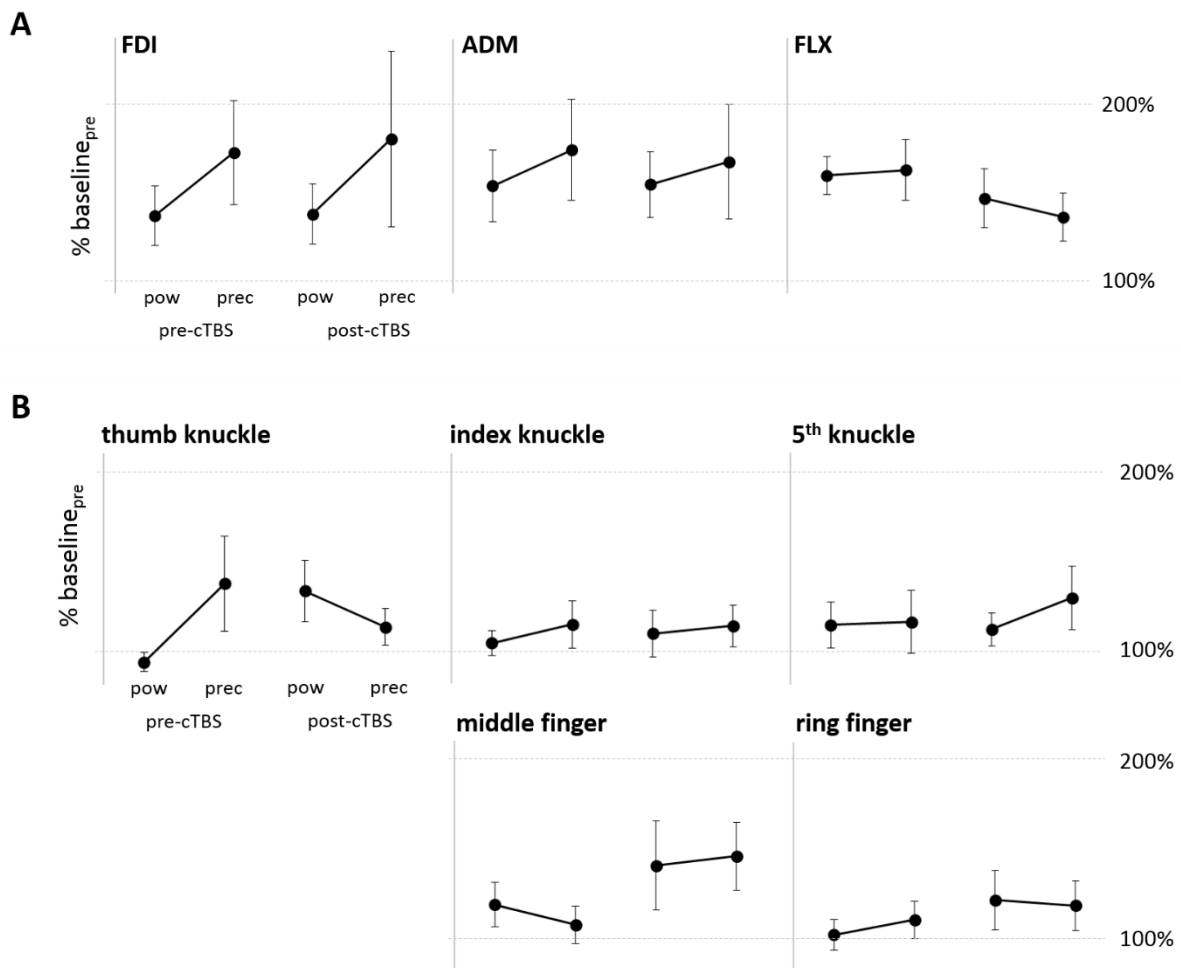
Figure C4: Effects of cTBS on AOEs.

Mean and standard error of FDI, ADM and FLX MEPs (A) and middle, ring, thumb knuckle, index knuckle and 5th knuckle MEKs (B), as a function of grasp type (precision (prec), power (pow)) at timing t_2, before (left side) and after (right side) cTBS protocol over M1. All values are expressed as a % of the average of baseline$_{pre}$ for each session.
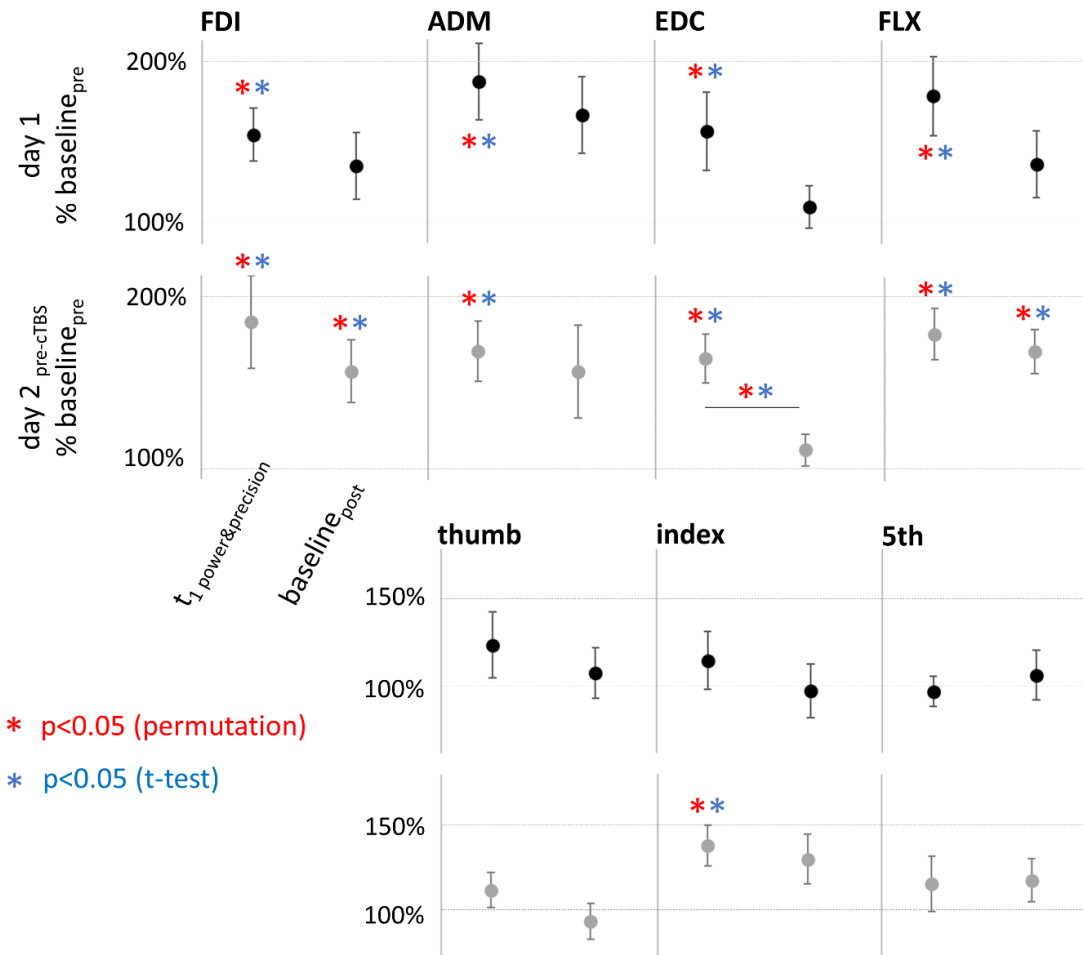
Figure D1: Generic attentional effects on MEPs and MEKs amplitude.

Mean and standard error for the four muscles (FDI, ADM, FLX, and EDC) MEPs and three elevation angles MEKs (thumb, index and 5th) are shown as a percentage (%) of the average of baseline$_{pre}$ on the y-axis. The two sessions are stacked vertically for each measure (day1 on top, day2$_{pre-cTBS}$ on bottom). The baseline$_{pre}$ level is represented by the low horizontal bar (100%). The 2 phases contrasted (timing $_{1pow\&prec}$, baseline$_{post}$) are shown on the x-axis. Significant differences with baseline$_{pre}$ are represented by an asterisk in the top of the value, between the two phases by a horizontal segment surmounted by an asterisk (red for permutation test, blue for classical parametric test; $p<0.05$).
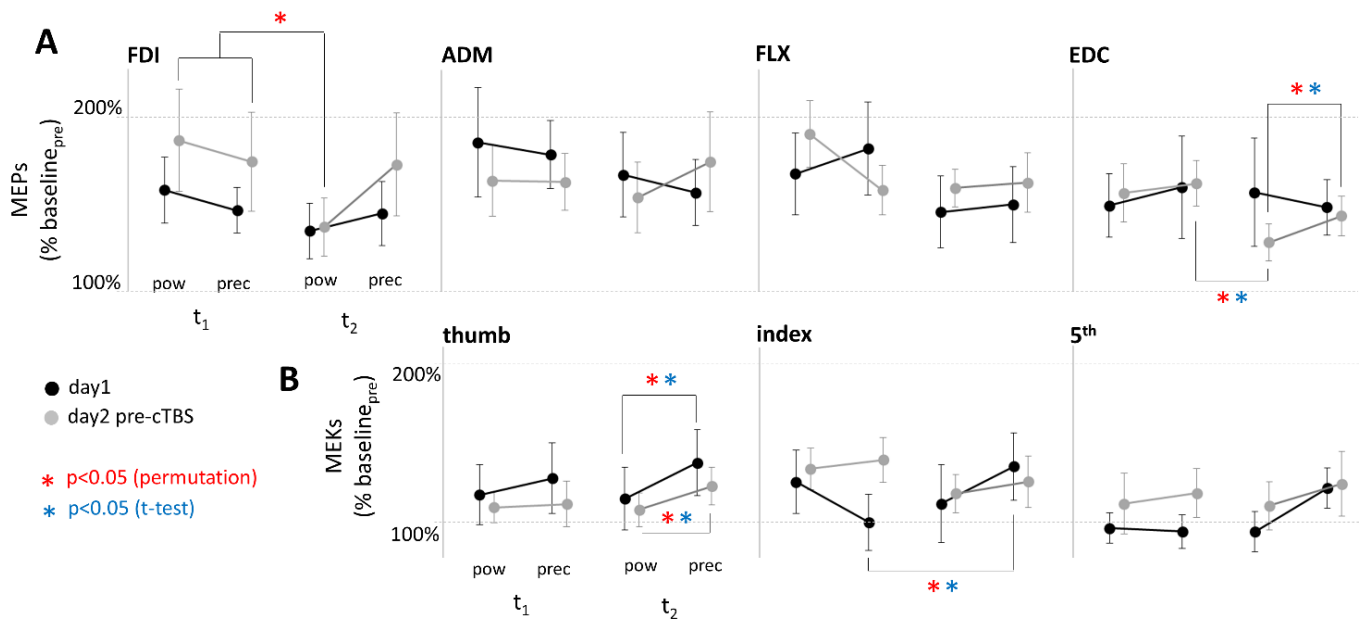
Figure D2: Action observation effects on MEPs and MEKs amplitude.
Mean and standard error of the four muscles (FDI, ADM, FLX, and EDC; panel A) and MEKs (thumb, index and 5th; panel B) expressed as a % of the average of baseline_{pre}, separately for session (day 1, day 2_{pre-cTBS}), timing (t_1, t_2), and grasp type (precision (prec), power (pow)). Significant differences are represented by an asterisk (red for permutation test, blue for classical parametric test; p<0.05).
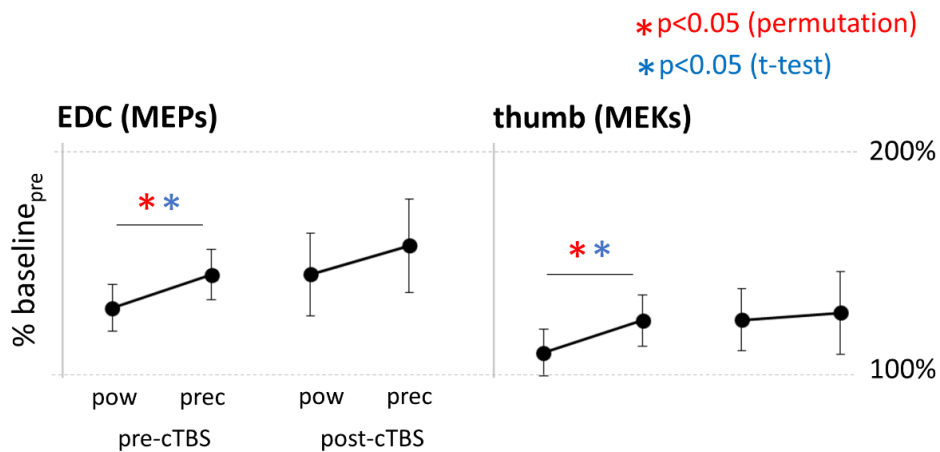
Figure D3: Effects of cTBS on AOEs.
Mean and standard error of EDC MEP and thumb MEK, as a function of grasp type (precision (prec), power (pow)) at timing t_2, before (left side) and after (right side) cTBS protocol over M1. All values are expressed as a % of the average of baseline_{pre} for each session. Significant differences are represented by an asterisk (red for permutation test, blue for classical parametric test; p<0.05).
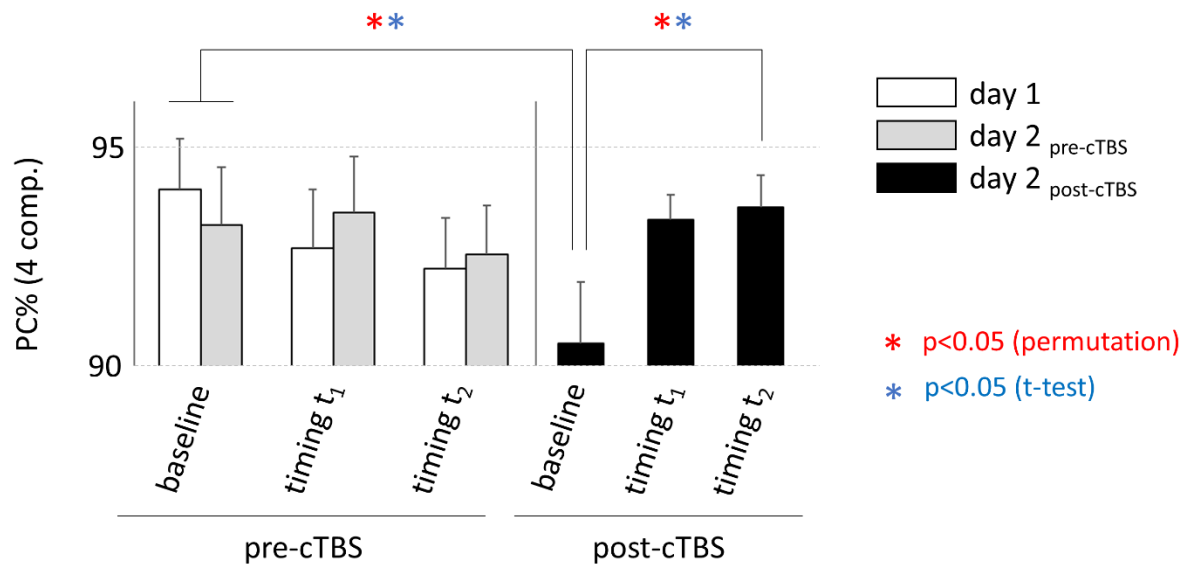
Figure D4: Whole hand configuration changes across sessions and conditions.
PC% values of the fourth first components (y-axis), computed on the 8 elevation angles, are shown for baseline and AO trials (baseline, timing 1 and timing 2) for the three sessions (day 1, day 2 pre-cTBS, day 2 post-cTBS). Significant differences are represented by an asterisk (red for permutation test, blue for classical parametric test; p<0.05).

2. Study 2: Motor recruitment during action observation: effect of interindividual differences in action strategy

Visual processing of other's actions is supported by sensorimotor brain activations. Access to sensorimotor representations may, in principle, provide the top-down signal required to bias search and selection of critical visual features. For this to happen it is necessary that a stable one-to-one mapping exist between observed kinematics and underlying motor commands. However, due to the inherent redundancy of the human musculoskeletal system, this is hardly the case for multi-joint actions where everyone has his own moving style (individual motor signature IMS). Here we investigated the influence of subject's IMS on subjects' motor excitability during the observation of an actor achieving the same goal by adopting two different IMSs. Despite a clear dissociation in kinematic and electromyographic patterns between the two actions, we found no group-level modulation of corticospinal excitability (CSE) in observers. Rather, we found a negative relationship between CSE and actor-observer IMS distance, already at the single-subject level. Thus, sensorimotor activity during action observation does not slavishly replicate the motor plan implemented by the actor, but rather reflects the distance between what is canonical according to one's own motor template and the observed movements performed by other individuals.

My Contribution: protocol definition, data recording and analysis, results interpretation and manuscript writing

This work is currently submitted in ELife:

The coordination of our own actions with those of others requires the ability to read and anticipate what and how our partner is about to do. Indeed, when observing someone else moving, we can extract useful information such as future bodily displacements (Blakemore and Frith 2005; Falck-Ytter, Gredebäck, and Von Hofsten 2006; Flanagan and Johansson 2003) or infer higher-order cognitive processes hiding behind those actions (Becchio et al. 2008; Soriano et al. 2018). In principle, knowledge about the invariant properties of movement control (Flash and Hogans 1985; Bennequin et al. 2009) could support inferences about the unfolding of other's actions (Casile et al. 2010; Dayan et al. 2007). In this regard, it has been proposed that these inferences may be based on a direct match between actor's sensorimotor activations during Action Execution (AE) and observer's sensorimotor activations triggered by AO (Rizzolatti and Craighero 2004; Rizzolatti, Fogassi, and Gallese 2001; Rizzolatti and Sinigaglia 2016). Indeed, using TMS-evoked CSE, motor recruitment during AO was shown to automatically mirror the sequence of motor commands implemented by the actor (for a review please see: (Naish et al. 2014)).

This idea is however challenged by the redundancy that characterizes the organization of human movement (Kilner 2012; D'Ausilio, Bartoli, and Maffongelli 2015a; Hilt et al. 2017). The abundance of degrees of freedom available during AE suggests that different joint configurations, as well as spatio-temporal patterns of muscle activity, can equally be used to reach the same behavioral goal (Bernstein 1967). In this regard, the direct-matching hypothesis (Rizzolatti, Fogassi, and Gallese 2001; Rizzolatti and Craighero 2004; Rizzolatti and Sinigaglia 2016) explains inferences when a direct relationship exists between muscle recruitment, movement kinematics and behavioral goals (e.g. simple finger movements). However, it is less clear how this proposal deals with the observation of complex movements (i.e. multi-joint movements). In this case, any sensorimotor-based inference about other's actions, amount to finding a solution to a many-to-many mapping problem.

Here we suggest that a simpler mapping exists between behavioral goals and the lower dimensionality space of whole-body configurations (i.e. synergies; (Hilt et al. 2017)). In fact, although a handful of kinematic solutions are biomechanically valid, everyday actions (i.e. reaching for an object on the floor starting from a standing posture) are usually performed via a limited number of possible kinematic configurations of the biomechanical chain (e.g. "ankle" and "hip" strategies for postural control; (Berret et al. 2009; Horak and Nashner 1986)). On the top of that, each individual carry his own robust and yet unique way of moving (Individual Motor Signature – IMS; (Hilt et al. 2016; Słowiński et al. 2016)). These two properties of human motor control may lead to a new one-to-one mapping that is function of everyone own way of moving (individual motor strategy, IMS). Backed

by this, we hypothesize that while observing others' multi-joint actions, people build sensorimotor-based predictions by referencing what they see to the motor engrams of their own IMS.

To verify our hypothesis, we asked naive participants to first perform and then observe a whole-body reaching action which could be executed with different IMSs. After characterizing subjects' own IMS during execution, we measured their sensorimotor recruitment (corticospinal excitability, CSE) by administering single-pulse Transcranial Magnetic Stimulation (TMS) on their motor cortex while they observed an actor achieving the same goal by using different IMSs (i.e. the participant's own IMS and a different one). CSE was measured from the cortical representation of the Tibialis Anterior muscle (TA) that shows a clearly dissociable pattern while executing the two IMSs.

According to a strong version of the direct matching hypothesis, all subjects requested to observe the actions should mirror the TA recruitment characterizing the actor (Fadiga et al. 1995; Fadiga, Craighero, and Olivier 2005; Naish et al. 2014). An alternative hypothesis predicts that CSE would reflect, on an individual basis, a measure of the distance between own IMS and observed IMS. Furthermore, if sensorimotor activations are greater for little IMS distance, then it is likely that the motor system is computing the similarity between observed and own IMS. On the contrary, a negative relationship, would suggest that sensorimotor inferences about other's goals might be built by computing the difference or an error measure between one's own motor template and the observed movement.

(b)   Materials and Methods

Participants

Twenty right handed volunteers (11 females and 9 males; age: 24 ±5 years) participated in the study. Data from 1 subject was removed due to technical problems during the experiment. None of the participants reported neurological, psychiatric or other contraindications to TMS (Simone Rossi et al. 2009). They had normal or corrected-to-normal visual acuity and were unaware of the purposes of the study. All of them gave informed consent before the experiment, which was approved by the Ferrara University/Hospital unified Ethics Committee and conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki, as revised in 1983.

Procedure and setups

The experiment was divided into three parts. Participants were first asked to perform the action execution task lasting ≅5 minutes. After that, the TMS procedure during the action observation task started (lasting ≅30 minutes). In the last part, participants were asked to repeat the action execution task. These two tasks are described below.
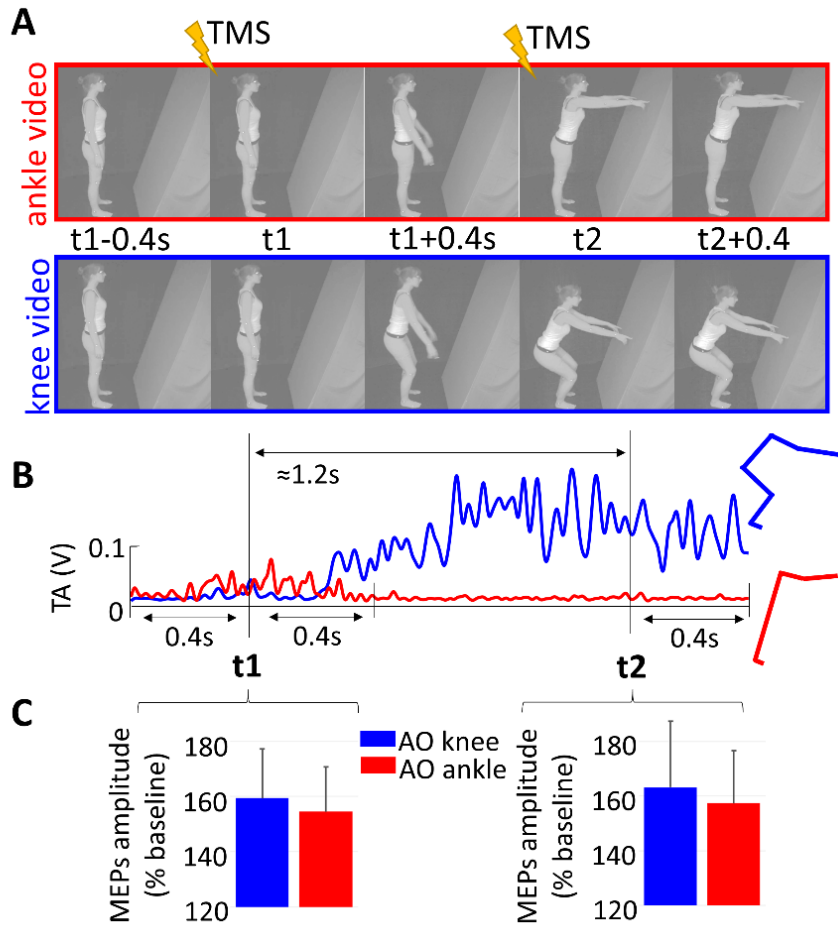
Figure 7: Stimuli illustration.

(A) Screenshots of the two AO task video-clips representing ankle and knee strategy. A single-pulse TMS was released at one of two different timings: t_1 (start of actor movement) and t_2 (end of actor movement) (B) Muscular activity of the actor right tibialis anterior (TA) for each motor strategy. At t_1, actor kinematics and TA activation are similar while at t_2, actor kinematics and TA recruitment are different across video-clips. (C) Average and standard error of normalized MEPs amplitude at t_1 and t_2 when observing the ankle (red) and knee (blue) video-stimuli. No group level MEPs modulation was present.

Action execution task

The action execution task was replicated from a previous study (Hilt et al. 2016) investigating the different motor strategies when pointing towards a homogeneous surface and without a specific target. This protocol was chosen because it keeps free the subjects from external constraints (e.g. a precise point to reach) and evokes natural inter-subject variability. Participants were asked to perform a series of whole-body pointing movements towards a uniform opaque curtain fixed to a wooden frame (2.5 tall × 1.5 m large; see Fig. 1) positioned at a 15° angle with respect to the vertical. The surface was soft enough to prevent subjects from using it as a support when finishing the movement but sufficiently elastic to keep its shape and remain flat. Subjects were told that they could point at

any position they wanted over the surface. Starting from a standing position and at a distance of 130% of arm's length from the surface, subjects had to move all body parts with the only constraint to keep the feet fixed and to move both arms simultaneously. The request to move the two arms together ensured that all markers lay approximately along the para-sagittal plane (Berret et al. 2009) to limit the kinematic analysis to this plane (right hemibody in 2D coordinates). All subjects were able perform the task. Ten trials were run before and after the action observation protocol.

More importantly, this protocol by avoiding external constraints (e.g. a precise target to reach), allow subjects to execute the movement they would naturally/spontaneously use (e.g. IMS). A previous study using this task observed a large movement variability across subjects but low intra-subject variability (Hilt et al. 2016). Interestingly, subjects behaviors were a trade-off between the optimization of two distinct cost functions. The first strategy (named Ankle) limits mechanical energy expenditure but uses a kinematic configuration that may be risky for equilibrium maintenance: bending the body forward using mainly ankle and shoulder joints while freezing knee and hip joints (large center of pressure forward displacement). In muscular terms, the ankle strategy is associated with a pre-activation of the tibialis anterior (anticipatory postural adjustment) followed by an inhibition of this muscle later in the movement (see Figure 7 in red). The second strategy (named Knee) increases mechanical energy expenditure but uses a kinematic configuration that may be safer for equilibrium maintenance: substantial knee flexion and forward trunk bending associated with a backward hip displacement (limited center of pressure forward displacement). In muscular terms, the knee strategy implied an activation of lower-leg muscles (including tibialis anterior) during the movement (see Figure 7 in blue).

Kinematic recordings. Whole-body movements in 3 axes (mediolateral, X; anteroposterior, Y; vertical, Z) were recorded using a seven cameras motion capture system (Vicon, Oxford, UK) sampling at 100 Hz. Eight retro-reflective markers (15 mm in diameter) were recorded. Markers were placed at the following anatomical locations on the right side of the body: the acromial process (named here "shoulder"), the lateral condyle of the humerus (named here "elbow"), the styloid process of the ulnar (named here "wrist"), the last phalanx of the index finger (named here "index"), the greater trochanter (named here "hip"), the knee interstitial joint space (named here "knee"), the ankle external malleolus (named here "ankle") and the fifth metatarsal head of the foot (named here "toe").

Electromyographic recordings. Electromyography (EMG) of left Tibialis Anterior muscle (TA; Figure 7B) was acquired from each subject via a wireless system (Aurion, ZeroWire EMG). The TA muscle was selected because it plays a central role in whole-body forward reaching execution

(Leonard, Brown, and Stapley 2009; Stapley, Pozzo, and Grishin 1998). Before electrodes placement, the skin was shaved and cleaned with alcohol to obtain low impedance (< 5 kΩ). EMG signals were band-pass filtered (50–1000 Hz), digitized (2 kHz), acquired by a CED power1401 board and visualized with Signal 3.09 software (Cambridge Electronic Design, Cambridge, UK).

Action observation task

Stimuli. The experimental stimuli consisted in short video clips showing a lateral view of a female actor who executed the action following two different motor strategies, the Ankle strategy (in red, Figure 7) and Knee strategy (in blue, Figure 7). The kinematic data of the actor was measured as previously described for the Action execution task. Movement onset and offset times were defined as the instant at which the linear tangential velocity of the index fingertip passed respectively above or below 5% of the peak value obtained during the reaching movement. Duration of the two movements were around 1.2sec. Video-clips started 400ms before the beginning of the movement and finished 400ms after the end of it (Figure 7B), for a total length of around 2sec. Electromyography (EMG) of the actor left TA (Figure 7B) and left Soleus (SO) were also acquired (for more details, see "Action execution task" – *"Electromyography recordings"*). Activities of the two muscles for each stimulus are presented in Supplementary Material E.

Procedure. Subjects were seating in a comfortable armchair with their legs resting. A 17″ LCD computer monitor (1024×768 pixels; refresh rate 60Hz) was placed at a distance of 60 cm from their frontal plane. Each trial started with the presentation of a grey central fixation cross displayed on a black screen. After 3s, a video-clip appeared. During each video-clip a single-pulse TMS was released at one of two different timings. The first (t_1) corresponded to the start, the second (t_2) to the end of the movement shown in the video-clips. Defined in this way, the two timings refer to very distinct moments in term of kinematic and muscular activities. At t_1, actor body posture is similar across video-clips (Figure 7A), while TA muscular anticipatory activations are present in the ankle strategy only (Figure 7B). By contrast, at t_2 actor kinematics are different across video-clips (Figure 7A), and TA is inhibited in the ankle strategy while remains active in the knee strategy (Figure 7B). At the end of each trial, an attentional question appeared on the screen (for more details see Supplementary Material F). In total, 80 trials were presented: 2 video stimuli X 2 timings of stimulation X 20 repetitions. Twenty baseline trials were recorded at rest (eyes closed, subjects imagining a relaxing landscape) half at the beginning and half at the end of the session. The presentation of the stimuli, the timing of the TMS pulses and response collection were controlled by Psychtoolbox Version 3.0 (PTB-3), implemented in MATLAB (The MathWorks Inc., Natick, MA, USA).

TMS and EMG recordings. Motor Evoked Potentials (MEP) were recorded with a wireless EMG system (Aurion, ZeroWire EMG) from the left Tibialis Anterior (TA). Before electrodes placement,

the skin was shaved and cleaned with alcohol to obtain a low impedance (< 5 kΩ). EMG signals were band-pass filtered (50–1000 Hz), digitized (2 kHz), acquired by a CED power1401 board and visualized with Signal 3.09 software (Cambridge Electronic Design, Cambridge, UK). A 70 mm (loop diameter) figure-of-eight shaped conic coil connected to a Magstim stimulator (Magstim Co., Whitland, Dyfed, U.K.) was placed over the right primary motor cortex with antero-posterior directed current orientation. As optimum scalp position was considered the location on the scalp where maximum amplitude MEPs in the TA were evoked at the lowest possible stimulation intensity (hotspot). Once the optimal site was found, the scalp was marked with a felt pen to ensure consistency between stimulations. The coil was secured by a lockable articulated arm (Fisso, Swiss). The resting Motor Threshold (rMT) was assessed by using standard protocols (5 out of 10 MEPs exceeding 50 μV peak-to-peak amplitude), with an inter-stimulus interval of about 8 seconds. During the experiment, single-pulse TMS was applied with an intensity of stimulation corresponding to 120% of the rMT.

Data analysis

Kinematic data. Kinematic trajectories were low-pass filtered using a digital fifth-order Butterworth filter at a cutoff frequency of 10 Hz. We focused the kinematic analysis on the final posture in the sagittal plane (Y, Z) that described the motor strategy used by the subject. Movement onset (t_{start}) and offset (t_{end}) time were defined as described earlier for the action video-clips. At t_{end}, four intersegmental angles were computed for the four principal joints used: ankle, knee, hip, and shoulder. These intersegmental angles were already used to characterize the motor strategies in previous studies (Hilt et al. 2016; for more details see Supplementary Material G).

IMS index. We computed an individual action execution index (IMS index) by normalizing (z-score) and averaging the final value of the four intersegmental angles considered. This index is a simple way to represent the final kinematic configuration of each subject and may thus be considered as description of the postural strategy implemented by each participant.

IMS distances. To complement the IMS index, we evaluated the difference/similarity between the IMS of each subject and the actor's implementation of the two IMSs. To this aim, we defined a distance by computing the root mean squared error (RMSE) between inter-segmental angular trajectories of the actor and each of the subjects. RMSE is commonly used to compute the average magnitude of the errors between experimental values and associated model predictions (Hilt et al. 2016).

$$RMSE = \sqrt{\frac{1}{N}\sum_{i=1}^{N} |\theta_{actor} - \theta_{subject}|}$$

All trials were time-normalized (from t_{start} to t_{end}) to 100 frames. For each subject and each joint (ankle, knee, hip, and shoulder) we computed an averaged angular trajectory that we compared (using RMSE) with the corresponding angular trajectory of the actor in both IMSs. RMSE were then normalized across subjects (z-score) and averaged across joints, to obtain a unique distance value for each pairwise comparison between subject's and actor's IMSs. From this point, $Dist_{ankle}$ and $Dist_{knee}$ will refer to the distance between the IMSs of subjects and the video-stimuli respectively showing the ankle strategy and the knee strategy.

Neurophysiological data. Trials with EMG activity in the 50ms period prior to TMS were discarded from the analysis (1% of the trials). Peak-to-peak value (mV) was used to represent MEP amplitude. MEPs exceeding 3 standard deviations (SD) from the mean peak-to-peak amplitude, at the single subject level, were excluded from the dataset (2% of the trials). The remaining MEPs were then averaged for every experimental condition and each subject. To perform correlation with IMS, we computed and normalized (z-score) the subtraction of the MEPs amplitude recorded when observing the video stimulus 1 (ankle strategy) from the MEPs amplitude recorded when observing the video stimulus 2 (knee strategy), for each subject (i.e. $MEPs_{AO-knee} - MEPs_{AO-ankle}$). This subtraction will be further called action observation index (AO index). Computed in this way (see Figure 8C): a negative value of AO index indicates a greater CSE modulation when observing knee stimulus compared to ankle stimulus, a positive value of AO index indicates a greater CSE modulation when observing ankle stimulus compared to knee stimulus, and an AO index close to null indicates similar CSE modulation when observing the two stimuli.

Statistical analysis

We used Shapiro-Wilk test to check the normality assumption for parametric tests. MEPs data and kinematic parameters were not normally distributed ($p<0.05$) and we then decided to use a two-tail permutation test (5000 permutations; Matlab function *mult_comp_perm_t1*).

All preprocessing and analyses were performed using custom software written in Matlab (Mathworks, Natick, MA, USA). For each correlation analysis, we estimated the Pearson correlation coefficient (R) and the associated p-value (Matlab function *corcoeff*). The data used in the correlation analysis were all normally distributed according to Shapiro-Wilk test ($p>0.05$). All P-values were corrected for multiple comparisons using the Benjamini-Hochberg False Discovery Rate (Matlab function *fdr_bh*).

(c)   Results

Action execution task

No significant changes in the execution task appeared between the two repetitions of the same action execution task, before and after action observation. This was verified on the final posture achieved by participants (IMS) and on the measure of IMS distance with respect to actor's IMSs ($Dist_{knee}$ and $Dist_{ankle}$; for values and statistics refer to Supplementary Material H and I). Additionally, and in agreement with previous results (Hilt et al. 2016), IMSs showed large between-subjects and small within-subject variability (Supplementary Material H). Furthermore, as already shown earlier (Hilt et al. 2016)., we found a significant negative correlation between the two distances ($Dist_{knee}$ vs $Dist_{ankle}$; $R=-75$, $p<0.01$; Supplementary Material J), such that the more a subject had an IMS close to one of the two strategies, the further away will be from the other. This confirms that the two selected IMSs are likely the two ends of a natural behavioral continuum. Also, no correlation was found in our experimental subjects (Supplementary Material K) between TA activation at t_2 and kinematics of the final posture (AE index) suggesting that a many-to-many mapping indeed exists between muscle pattern and movement kinematics.

Action observation task

Subjects answered correctly to the attentional question in most of the trials (90% ±8). Regarding CSE, a significant decrease was observed in the baseline computed after action observation (0.34$\pm$0.07V) compared to before (0.43$\pm$0.10; $t=2.88$, $p<0.01$). A change of baseline before and after observation has already been described and commented in (Hilt et al. 2017). Furthermore, we found a significant increase of MEPs amplitude in the trials recorded during action observation (average of the four conditions: 0.53$\pm$0.10V) compared to baseline pre ($t=-2.15$, $p<0.05$) and post ($t=-4.25$, $p<0.01$). These variations are associated to an unspecific action observation effect, which may be explained by a generic arousal effect (see (Hilt et al. 2017)). Rather, the specificity of the action observation task has to be verified across conditions (timing of TMS and properties of the action stimuli). When normalizing on the averaged baseline pre and post, no significant difference was observed between the four experimental conditions: t_{1knee} (1.59$\pm$0.18%), t_{1ankle} (1.55$\pm$0.16%), t_{2knee} (1.63$\pm$0.24%), t_{2ankle} (1.57$\pm$0.19%). Equivalent non-significant results were found in normalizing the data on baseline pre. Since no kinematic cue is present in timing t_1, this condition may be used as an intra-experiment baseline. When normalizing the MEPs amplitude at t_2 by the average amplitude in t_{1knee} and t_{1ankle}, we obtained no significant differences between the two conditions (t_{2knee}: 1.01$\pm$0.05%, t_{2ankle}: 1.01$\pm$0.05%; $t=-0.10$, $p=0.93$). In conclusion, regardless of data normalization choice, no group level significant effects were present between the different conditions.

Correlations between IMS index and CSE modulation

To further evaluate the link between IMS and CSE modulation we ran a correlation analysis between the IMS recorded during the action execution task of each subject and the AO indexes (difference between MEPs amplitudes in the two action observation conditions). A significant correlation was found between IMS and the AO index on timing t_2 only (t_1: R=-12, p=0.94; t_2: R=-73, p<0.01; Figure 8). Equivalent results were found when separating for the IMS recorded before (t_1: R=-1, p=0.99; t_2: R=-70, p<0.01) and after AO (t_1: R=-22, p=0.94; t_2: R=-63, p<0.01). This result suggests that only in the presence of discriminative kinematic cues (t_2), CSE modulation to AO depends on IMS.
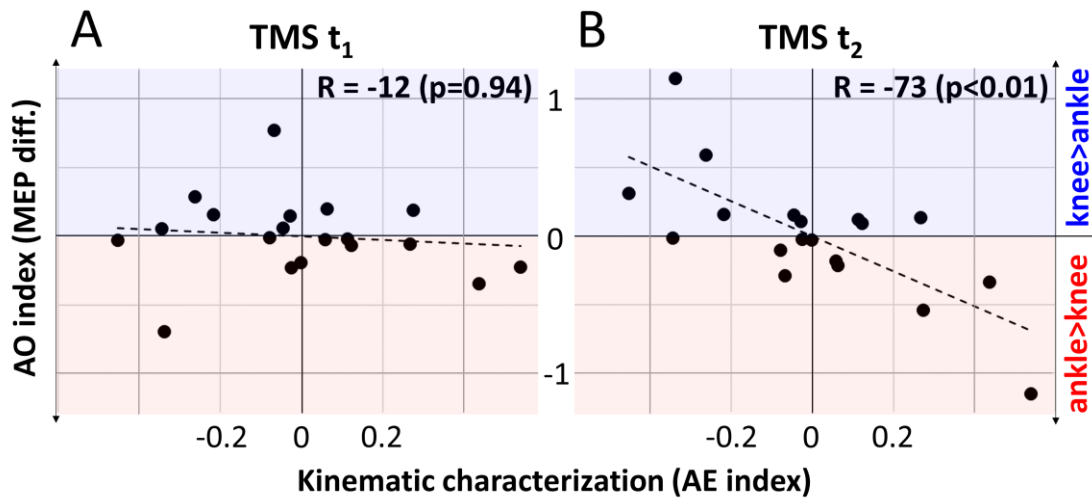
Figure 8: Correlation between action execution and action observation index indexes.
Correlation between the action execution index (AE index) and the action observation index (AO index) at TMS timing t_1 (A) and t_2 (B). A negative AO index value (lower part – red background) indicate larger corticospinal excitability when observing ankle IMS compared to knee IMS, and vice versa for positive values (upper part – blue background). Pearson correlation coefficients and p-values are reported above each graph.

Correlations between IMS distance to stimuli and CSE modulation

To complement absolute IMS information, we defined a distance measure ($Dist_{ankle}$ and $Dist_{knee}$) that evaluates the difference/similarity between the IMS of each subject and the two IMSs implemented by the actor (two video-stimuli). We analysed these distances in relation to the AO index. The correlation analysis at timing t_2 revealed two significant correlations, in opposite directions. The AO index is negatively correlated with $Dist_{knee}$ (R=-65, p<0.01; Figure 9A) and positively correlated with $Dist_{ankle}$ (R=59, p<0.05; Figure 9B). In other terms, subjects exhibited larger MEPs amplitude when observing the action that differed the most from their own IMS (Figure 10). No significant correlation was present at t_1 ($Dist_{knee}$: R=-3, p=0.90; $Dist_{ankle}$: R=26, p=0.37).

The same significant effect was found when using distances computed from pre-AO data (AOt_1 – $Dist_{ankle}$: R=-3, p=0.91; AOt_1 – $Dist_{knee}$: R=15, p=0.54; AOt_2 – $Dist_{ankle}$: R=-57, p<0.05; AOt_2 – Dist

knee: R=57, p<0.05). Differently, using distances computed from post-AO, no significant correlation was observed (AOt$_1$ Dist $_{ankle}$: R=-3, p=0.89; AOt$_1$ Dist $_{knee}$: R=31, p=0.18; AOt$_2$ Dist $_{ankle}$: R=-44, p=0.11; AOt$_2$Dist $_{knee}$: R=-42, p=0.14). This absence of significant correlation (despite a trend similar to pre-AO) revealed a slight change during the AO task (already suggested by the change of CSE between baseline pre and post-AO).
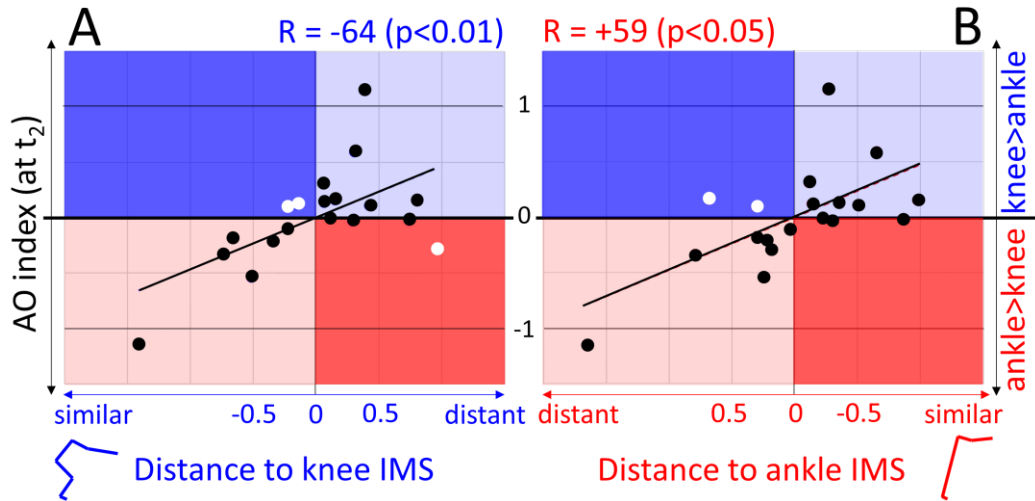
Figure 9: Correlation between distances to each stimulus and the AO index at TMS timing t$_2$.
The Pearson correlation coefficients and p-values are reported on each graph. Each graph (A, B) can be separated into four regions. The blue region indicates subjects exhibiting a higher CSE when observing knee IMS video-clip compared to ankle IMS video-clip. The red region indicates the position of subjects exhibiting a higher CSE when observing ankle IMS video-clip compared to knee IMS video-clip. Darker areas indicate subjects exhibiting greater CSE when observing their own IMS. On the opposite, lighter areas (and black points) indicate subjects exhibiting greater CSE when observing the IMS opposite to their own behavior in AE.

(d)   Discussion

Previous studies on action observation mostly investigated mirroring mechanisms evoked by simple goal-directed actions (i.e. involving few degrees of freedom) performed in the canonical way. However, due to motor redundancy, observation of daily life actions is rarely characterized by a univocal relationship between the visual (e.g. observed kinematics) and the motor description (e.g. underlying motor commands) of the action. For the same reason, it is not clear how the predictions about others' actions (multi-joint) would be simplified by a direct access to the motor commands (e.g. muscle-level).

To better understand these mechanisms in the context of multi-joint actions, we investigated observers' motor excitability while seeing two different motoric variants of a whole-body reaching action. To this purpose we selected the cortical representation of TA muscle, differentially involved in the variants of the IMS used to achieve the goal. During execution of the first variant (ankle IMS),

TA is activated only in anticipation of the movement onset (at t_1, Figure 7A). In the second variant (knee IMS), TA becomes active only after the initiation of the movement (at t_2, Figure 7A). Group-level analysis did not find any significant difference in CSE modulation, mainly because of a huge inter-subject variability. In agreement with this result, several authors recently reported a quite large inter-subject variability in CSE modulations to AO (Palmer et al. 2016; Hilt et al. 2017; Hannah, Rocchi, and Rothwell 2018). This large inter-subject variability may have multiple origins. As we argued earlier, one possibility is that the lack of a clear muscle-to-movement mapping in complex actions, leads to mixed results when we observe CSE modulations at the group level. Inter-subject variability increases with task complexity. Indeed, a simple motor task (e.g. finger's abduction/adduction) is characterized by a simple and unique motor mapping directly translated into coherent group-level AO effects (e.g. (Romani et al. 2005)). In more complex actions involving a larger number of degrees of freedom (e.g. upper-limb reaching to-grasp movement), the mapping depends upon individual strategies leading to larger inter-subject variability. These facts may explain why we did not find robust group-level CSE modulations to complex AO (Palmer et al. 2016; Hilt et al. 2017; Hannah, Rocchi, and Rothwell 2018). In other words, our results indicate that CSE-based measures of sensorimotor activations during others' (complex) action observation are subject-dependent and cannot be summarized into a common standard pattern. When CSE data were analysed at the single subject level, a clear result emerged. CSE was modulated at the single subject level according to the "distance" between actors' and observer's IMS: larger CSE modulations are associated with the observation of a more different IMS (Figure 10).
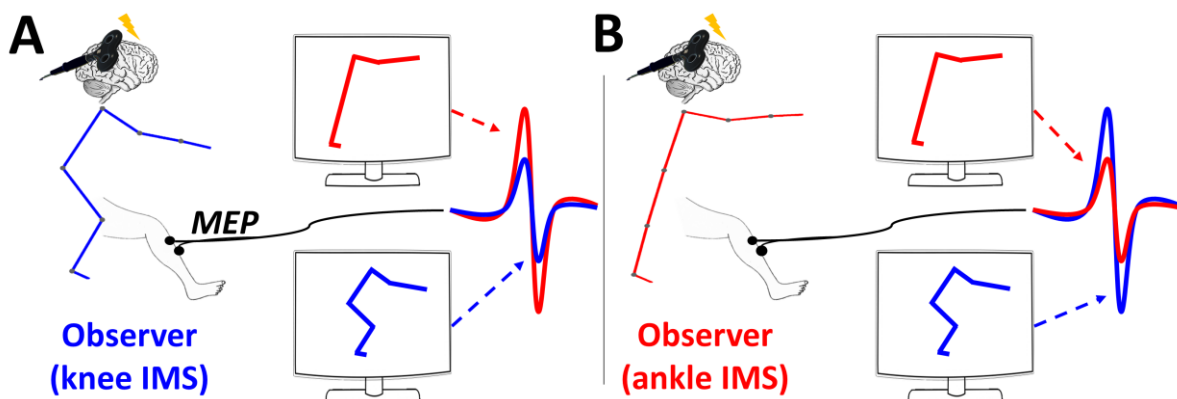
Figure 10: Illustration of the main results.

MEPs amplitudes are depicted when observing knee (blue stick figure) or ankle (red stick figure) stimulus, for a subject that performed the knee (A) or the ankle (B) IMS in AE. Our results showed that corticospinal excitability was greater when actor and observer IMSs differ the most. These results agree with the predictive coding hypothesis that hypothesize the existence of a distance computation between observed movement and observer's IMS.

Neurophysiological studies conducted on experts have also shown a relationship between sensorimotor recruitment and motor familiarity or similarity with other's action (i.e. sport players: (Aglioti et al. 2008), musicians: (Candidi et al. 2014; D'Ausilio et al. 2006), dancers: (Calvo-Merino et al. 2005; Calvo-Merino et al. 2006; Jola et al. 2012)). This body of research seems to suggest a positive correlation between the amount of sensorimotor activity while observing skilled actions, and the individual expertise in that skill. These findings seem to contradict what we found in the present experiment. However, it is important to bear in mind the fundamental difference existing between common everyday actions (as in our study) and overtrained ones (as in studies with experts). In fact, extensive and highly specific training isolate one skillset also by reducing generalization to adjacent ones (negative transfer: (Ajemian et al. 2010; R. A. Schmidt and Lee 1999; R. A. Schmidt and Young 1986)). In this regard, expertise could amount to a greater ability to compute very precise distances in one specific skill only (Aglioti et al. 2008). At present, we show evidence that the sensorimotor system, while observing complex but perfectly common whole-body actions, computes differences rather than similarities.

At this point, it is important to discuss how CSE modulations translate into sensorimotor activities capable of supporting inferences about others' action. Our results are at odds with a simulative account of other's action during discrimination by challenging the claim that a direct matching of the actor's kinematic and/or muscular activities does take place in the observer's motor system. Instead, the fact that sensorimotor activities during AO are shaped around a measure of error between observed and own IMSs, agrees with the predictive coding framework. In this model, prior motor knowledge provides critical top-down signals that are integrated with bottom-up sensory-based processing (Friston 2010b; Friston, Mattout, and Kilner 2011). To do so, a comparison between predicted and observed kinematic information generates a prediction error signal that is used to update the representation of other's action. Neurophysiological studies on simple goal-directed actions indicated that sensorimotor recruitment during AO reflect a prediction error signal (Aglioti et al. 2008; Candidi et al. 2014; Cardellicchio et al. 2018). Interestingly, previous behavioral studies found an increase in perceptual discrimination performance of other's actions, when actor-observer motor distance was small (Koul et al. 2016; Macerollo et al. 2015). From these data, we speculate that actor-observer similarity may induce smaller prediction errors, and consequently more accurate perceptual performances. On the opposite side, large actor-observer IMS distance is associated to a decline in perceptual performance (Koul et al. 2016; Macerollo et al. 2015) while sensorimotor activations increased, possibly playing a compensatory role (D'Ausilio et al. 2014; Schmitz et al. 2018; Bartoli et al. 2015). In other words, a greater uncertainty about other's action will call for a greater need of trustful predictions and consequently recruit to a greater extent the sensorimotor areas. In this context,

the present study adds direct neurophysiological evidence that prediction errors are estimated by accessing IMS-related information.

Our results suggest that the many-to-many mapping problem in other's (multi-joint) action discrimination might be solved by accessing knowledge about IMSs. Indeed, the stability of IMSs (Coste et al. 2017; Słowiński et al. 2016) may reflect the implicit control and prioritization of a limited number of internal parameters during action planning and execution, partly solving the motor redundancy problem. In our task, individual anatomical differences contribute but do not fully explain the properties of the two IMSs (Hilt et al. 2016). More importantly, IMSs could derive from long-term processes of learning and adaptation to slow but constant changes of our body and neural circuits involved in the control of movements and sensations (Thoroughman and Shadmehr 2000; Thoroughman and Shadmehr 1999). Indeed, these neurobehavioral factors could be intertwined with other similarly important psychosocial aspects. For instance, the relatively small intra-subject variability observed in IMS (Hilt et al. 2016) could reflect variation in the emotional states of participants which are discriminable by an attentive observer (Montepare, Goldstein, and Clausen 1987). On the other hand, the relative stability of IMS may be associated to personality traits (e.g. knee IMS was associated to increased anxiety (Carpenter et al. 2006) or even psychiatric condition (e.g. in schizophrenia (Slowiński et al. 2017)). These data are promising in the framework of developing experimental procedures to investigate individual behavior and complement group-level averaged results with potentially important idiosyncratic differences

In conclusion, we demonstrated that individual differences in the execution of a multi-joint action shape the sensorimotor activities during the observation of the same action. This shaping is made visible by our experimental design but should in principle be an ingredient of any multi-joint action. Beside the general suggestion that inter-subject variability should be considered as a tool rather than a problem, our results force us to redefine the core properties of the direct matching hypothesis. In fact, we propose that the AO Effects reflects sensitivity to differences rather than similarities with respect to other's behavior.

(e)   Additional data and analyses

E: Study 1.2: Actor's muscular activities
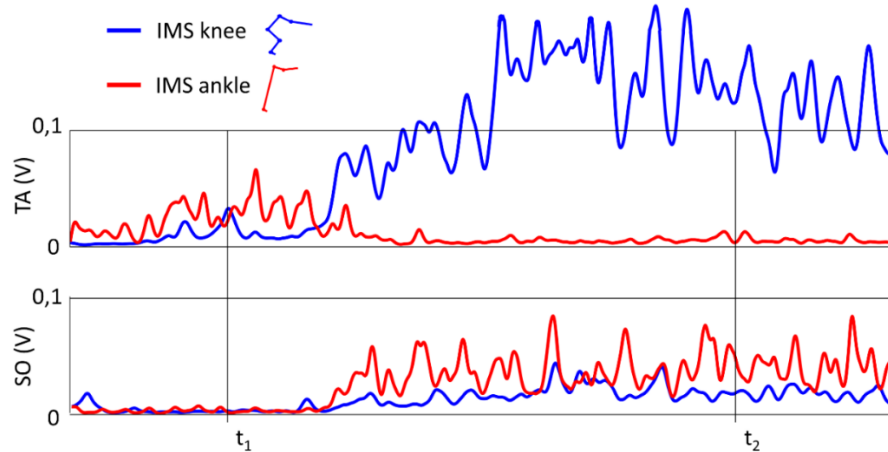
Figure E: Actor muscular activities.
Muscular activity of the actor right tibialis anterior (TA) and soleus (SO) for each video-clip: IMS knee (blue) and IMS ankle (red). Timing t_1 and t_2 at which single-pulse TMS were given are reported on each graph. At t1, TA activation is similar to the initial position and similar across video-clips. By contrast, at t2, TA recruitment is different across video-clips. These differences between timings and video-clips are less visible in SO. Therefore, TA was selected as the muscle of interest.

F: Study 1.2: Attentional questions

Three different questions could randomly appear, regarding the clip subjects just saw. Specifically, we asked what the final angle of the shoulder, hip or knee joint was, by offering two alternatives on screen. Two human silhouettes showed the two alternative postures, so that participants could indicate the correct answer by a computer mouse (i.e. left button click if the correct posture was displayed on the left side or right button click if the correct answer was shown on the right side of the screen). Responses were given with the right hand (ipsilateral to the stimulated motor area).
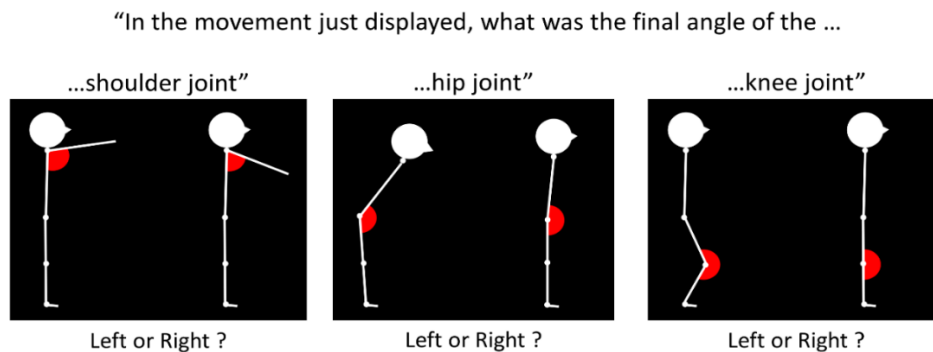
Figure F: Attentional questions.
Attentional questions were randomly presented at the end of each action observation trial, to ensure a good attentional level of all subjects to the stimuli. The question here are translated in English but were presented to subjects in Italian. Subjects had to press, with their right hand (ipsilateral to the stimulated motor area), on the left or right button of a mouse to indicate the side of the correct figure

(i.e. final angle). The correct answer could be presented either to the left or to the right side. Each type of question was shown and explained to the subjects before starting the experiment.

G: Study 1.2: Angles computation

We first defined five segments: foot (from toe to ankle), shank (from ankle to knee), thigh (from knee to hip), trunk (from hip to shoulder) and arm (from shoulder to elbow). We computed then the elevation angle (angle with the gravity's vertical) of each segment in the sagittal plane via the following equation:

$$\theta_{segAB} = \ tan^{-1}\left(\frac{B_y - A_y}{B_z - A_z}\right)$$

Where θ_{segAB} represents the elevation angle of the segment linking *A* to *B* having for cartesian coordinates in the sagittal plane (A_y, A_z) and (B_y, B_z) respectively.

Elevation angle are constrained by the anatomical limit of each joint, and never reach values higher (or lower) than *2π* (or *-2π* respectively). In 2D, knowing these constraints, intersegmental angles can be deduced directly from elevation angles. The intersegmental angle between the two segments Seg$_A$ and Seg$_B$ is equal to the subtraction of the elevation angle of Seg$_B$ to the elevation angle of Seg$_A$. Elevation and resulting intersegmental angles are illustrated in Supplementary Figure G left and right panel respectively.
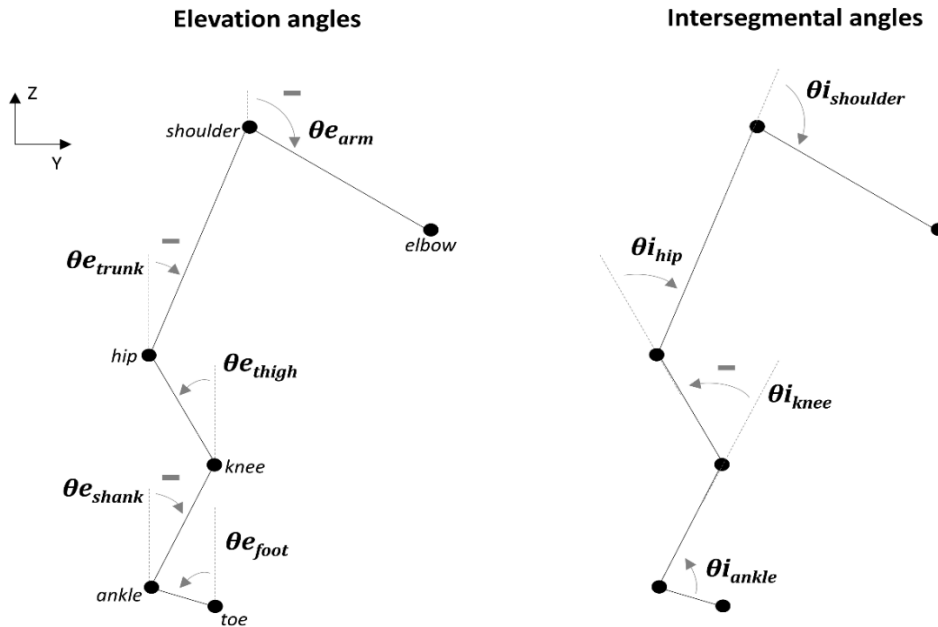
Figure G: Elevation angles computation.
Illustration of the computed elevation angles (left panel) and intersegmental angles (right panel) in the (Y,Z) plane. Angles are represented by a grey arrow. The sign "-" above an arrow indicates that the angle for this final posture is negative. Kinematic markers are represented by black dots.
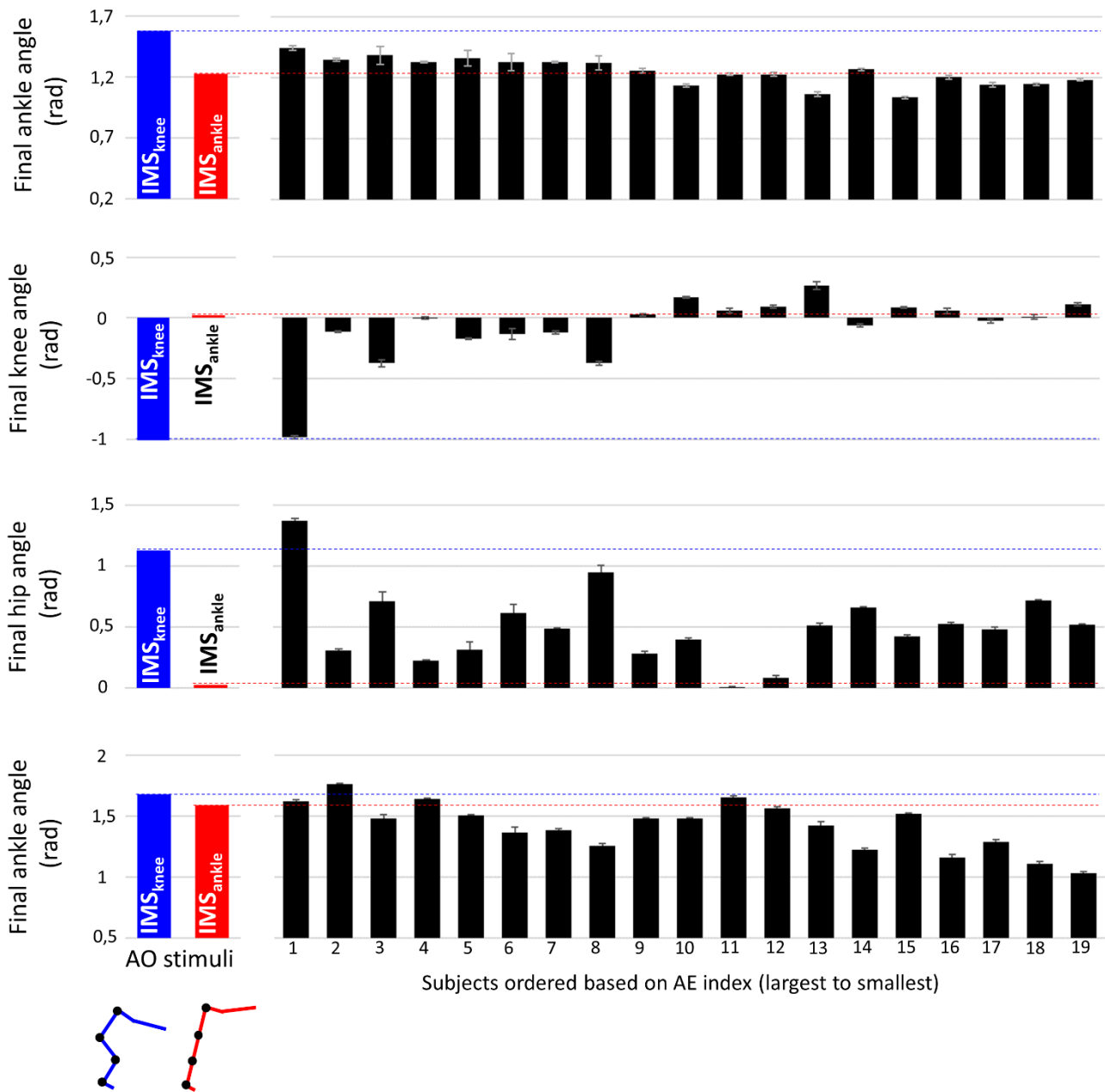
Figure H: Detailed subjects' intersegmental angular values

Final intersegmental angular values for each subject (1 to 19; ordered from the largest to the smaller AE index) and each joint (ankle, knee, hip, shoulder), averaged across AE trials (pre and post AO). For each subject, standard error encompasses the variability across trials and session (pre and post AO). As a reference, we added the corresponding value for each stimulus (IMS_{knee}, IMS_{ankle}). No standard error can be computed for stimuli because they refer to one video (i.e. trial) of the actor. These graphs illustrate the expected large difference between subjects IMS and the small intra-subject variability (relatively small standard error).

Table H: Detailed subjects' intersegmental angular values and statistics.

Mean and standard error (across subjects) of the final intersegmental angles of the ankle, knee, hip and shoulder, extracted from the kinematics recorded in the action execution task pre-AO (left column), post-AO (right column). The third column presents the results of the permutation test comparing the values pre-AO and post-AO of each intersegmental angle.

Mean ±ste (rad)	pre-AO	post-AO	Statistic
Ankle	1.26 ±0.03	1.25 ±0.03	p=0.69, t=0.41
Knee	-0.09 ±0.08	-0.09 ±0.07	p=0.99, t=0.01
Hip	0.51 ±0.08	0.50 ±0.07	p=0.91, t=0.12
Shoulder	1.43 ±0.05	1.41 ±0.05	p=0.40, t=0.88

I: Study 1.2: Kinematic distances to stimuli values pre and post-AO

Table I: Detailed subjects' kinematic distances and statistics.

Mean and standard error (across subjects) of the kinematic distance between subject's and ankle (upper part) or knee (lower part) video-stimuli kinematics for the ankle, knee, hip and shoulder intersegmental angles. For each subject, these distances were computed via RMSE on the angular trajectories recorded during action execution task pre-AO (left column) and post-AO (right column). The third column presents the results of the permutation test comparing the values pre-AO and post-AO of each intersegmental angle.

Distance to ankle video-stimulus (RMSE)			
Mean ±ste (rad)	pre-AO	post-AO	Statistic
Ankle	4.6 ±3.6	5.9 ±4.2	p=0.41, t=-0.89
Knee	9.2 ±10.6	8.9 ±10.9	p=0.88, t=0.13
Hip	19.9 ±13.5	20.3 ±11.0	p=0.87, t=-0.17
Shoulder	55.5 ±38.0	50.9 ±34.1	p=0.10, t=1.66
Distance to knee video-stimulus (RMSE)			
Mean ±ste (rad)	pre-AO	post-AO	Statistic
Ankle	12.3 ±5.1	13.3 ±4.8	p=0.37, t=-0.96
Knee	39.8 ±12.8	39.4 ±11.1	p=0.91, t=0.13
Hip	28.9 ±12.3	28.7 ±9.0	p=0.94, t=-0.08
Shoulder	120.3 ±27.2	115.8 ±36.6	p=0.53, t=0.95

J: Study 1.2: Between distances correlation
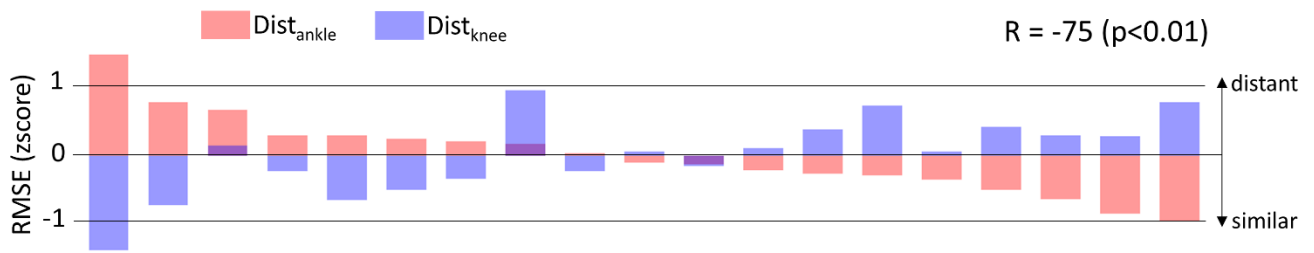
Figure J: Correlation between kinematic distances.
Individual distances to each video-stimulus (red: to ankle stimulus, blue: to knee stimulus), ordered in function of distance to ankle stimulus (Dist$_{ankle}$). Due to z-score normalization, negative values represent small distances to stimulus (i.e. high similarity) while positive values large distances (i.e. high discrepancy). Distance to the two actor's kinematics configurations were defined by computing the root mean squared error (RMSE) between inter-segmental angular trajectories of the actor and each of the subjects. RMSE were normalized and averaged across joints to obtain a unique distance value for each pairwise comparison between subject's and actor's IMSs.

K: Study 1.2: Subject's TA muscle activity during AE
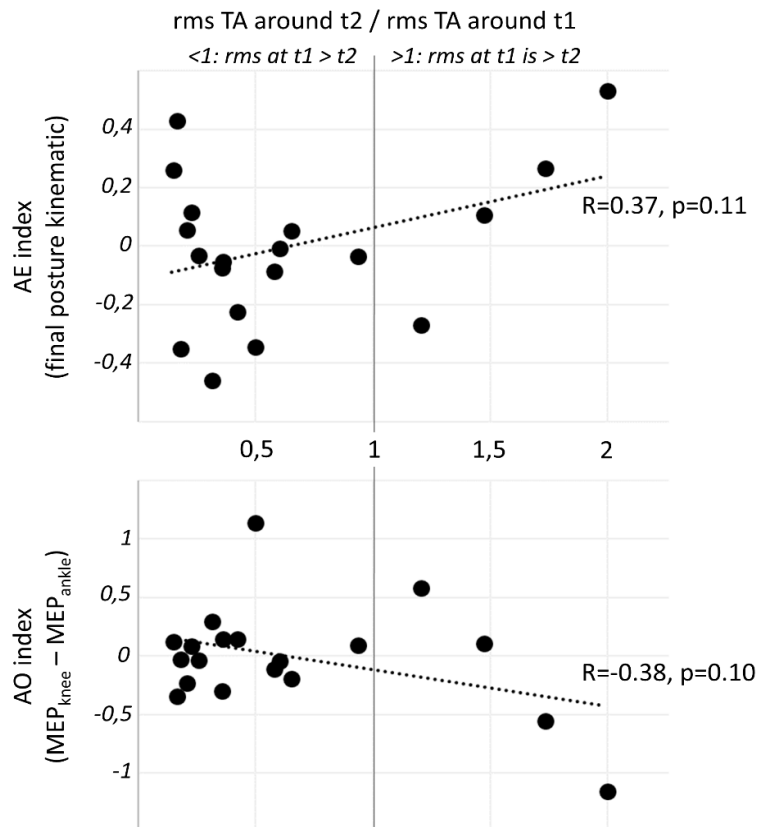
Figure K: Tibialis Anterior activity in function of kinematic strategies.
For each subject, we recorded tibialis anterior (TA) activity during the action execution part. Data were redressed, centered and low-pass filtered (Butterworth filter, order 5, cut-off: 20Hz). In this analysis, we verified the link between TA activity and kinematic strategy. For each trial (of each

subject), we computed the ratio between the root mean square value on a 50ms a window around t_2 (finger's movement offset; from t_2-25 to t_2+25) on the one around t_1 (finger's movement onset; from t_1-25 to t_1+25). Before computing an average value for each subject, we discarded values exceeding the mean by 2 standard deviations (i.e. outliers) within subject. If the value is greater than 1, the TA muscle is more activated in t_2 compared to t_1, and the opposite for values inferior to 1. In a first correlation analysis (upper panel), we compared this ratio to our AE index, characterizing each subject final posture kinematic. A positive trend is present but no significant correlation. This suggests the absence of a clear linear link between subject's kinematics and the activity of the principal leg muscle of this movement (i.e. no one-to-one mapping). Similarly, when comparing this ratio with our AO index, a negative trend appears, but no significant correlation.

3. Study 3: Early modulation of intra-cortical inhibition during the observation of action mistakes

Errors while performing an action are fundamental for learning. During interaction others' errors must be monitored and taken into account to allow joint action coordination and imitation learning. This monitoring relies on an action observation network (AON) mainly based on parietofrontal recurrent circuits. Although different studies suggest that inappropriate actions may rapidly be inhibited during execution, little is known about the modulation of the AON when an action misstep is shown. Here we used single and paired pulse transcranial magnetic stimulation to assess corticospinal excitability, intracortical facilitation and intracortical inhibition at different time intervals (120, 180, 240 ms) after the visual presentation of a motor execution error. Results show a specific and early (120 ms) decrease of intracortical inhibition likely because of a significant mismatch between the observed erroneous action and observer's expectations. Indeed, as proposed by the top-down predictive framework, the motor system may be involved in the generation of these error signals and our data show that this mechanism could rely on the early decrease of intracortical inhibition within the corticomotor system.

My Contribution: protocol definition, data recording and analysis, results interpretation and manuscript writing

This work was published in Scientific Reports:
P Cardellicchio, PM Hilt*, E Olivier, L Fadiga and A D'Ausilio (2018) Early modulation of intra-cortical inhibition during the observation of action mistakes. Scientific Reports, 8(1): 104-118 (* co-first author)

This work has been presented as on oral communication in the International Organization of Psychophysiology Congress (4-8 september, 2018, Lucca, Italy):
A D'Ausilio, P Cardellicchio, E Dolfini and PM Hilt. Motor processes in a multi-agent environment.

(a)   Introduction

In everyday life, while interacting with others, we continuously infer their intentions (Becchio et al. 2012) through a combination of bottom-up and top-down processing particularly sensitive to action goals (Bekkering et al. 2009; Botvinick et al. 2001; Vesper et al. 2010). Thus, fast and effective detection of action errors is fundamental for flexible adaptation to other's behavior and provides essential support for social learning (Botvinick et al. 2001). The literature on action error observation has indicated that different brain regions may be active during error observation. In particular, different parts of the medial prefrontal cortex are active during the observation of unusual actions (Brass et al. 2007) depending on whether the observed behavior is intentional or not (Desmet and Brass 2015). At the same time, also simple action error observation elicits an electroencephalographic early error-related negativity (ERN; Bates, Patel, and Liddle 2005), similarly localized in medial-frontal structures (van Schie et al. 2004). However, other studies observed an increase of the P300 component probably associated with a more general monitoring process (De Bruijn, Schubotz, and Ullsperger 2007). The lateral premotor cortex is also activated within both hemispheres, although with a lateralization to the right, during the observation of both correct and erroneous actions (Manthey, Schubotz, and Von Cramon 2003). These activations could reflect a matching process between observed actions onto corresponding stored motor representations (Rizzolatti, Fogassi, and Gallese 2001). In this regard, some studies proposed that social action error detection may rely on our capability in sensing subtle kinematic violations in the observed action (Bond et al. 1992; Frank and Ekman 1997; Sebanz and Shiffrar 2009). According to this view, others' actions cues are compared to stored internal models of the same action to detect significant deviations (Wolpert, Doya, and Kawato 2003). Two different accounts propose two different alternatives to explain how this comparison takes place in the AON (Action Observation Network). The classic AON account suggests a direct matching between observer and actor (Rizzolatti, Fogassi, and Gallese 2001; Rizzolatti and Craighero 2004; Rizzolatti and Sinigaglia 2016) and thus observation of an error should activate the same inhibitory mechanisms at play during error execution (Buch et al. 2010). The predictive coding hypotheses suggests that the motor system computes the difference between expected and observed action-related information (Kilner, Friston, and Frith 2007; Urgen and Miller 2015; Sartori et al. 2015), and thus errors should activate the AON to a greater extent. However, while some studies have shown stronger facilitation in the AON when observing erroneous (Candidi et al. 2014; Senot et al. 2011), impossible or uncommon actions (Senot et al. 2011; Costantini et al. 2005; Koelewijn et al. 2008; Stapel et al. 2010; Abreu et al. 2012; Aglioti et al. 2008), other works show greater activity in the AON during observation of correct actions (van Schie et al. 2004; Shimada and Abe 2009; Shimada and Abe 2010; Avenanti et al. 2013). In this study, we investigated the

neurophysiological underpinnings of action error processing by focusing on its temporal dynamics. In fact, error processing may involve a cascade of neural events characterized by a temporally fine-grained balance between excitation and inhibition of specific motor programs. To this purpose, we used Transcranial Magnetic Stimulation (TMS) to measure primary motor cortex (M1) cortical and corticospinal excitability (Fadiga, Craighero, and Olivier 2005), at three time points (120, 180, 240 ms after action error). TMS timing was derived from a previous EEG investigation that shown an EEG error-related negativity (ERN) (van Schie et al. 2004; Wang et al. 2005; Gehring et al. 1993; Dehaene, Posner, and Tucker 1994) at about 120 ms latency and a correlated ERN feedback component (Nieuwenhuis et al. 2004; Talmi, Atkinson, and El-Deredy 2013) at about 250 ms latency after error occurrence. It is worth noting that 120 ms is also the earliest latency at which corticospinal excitability is modulated by graspable object observation (Franca et al. 2012). Specifically, we adopted single pulse (spTMS), short intracortical inhibition (sICI), and intracortical facilitation (ICF) protocols during the observation of picture sequences depicting either correct or erroneous actions. MEPs (Motor evoked potentials) evoked by spTMS provide an instantaneous read-out of the state of the motor system and had been widely used to investigate modulations related to action observation (Fadiga, Craighero, and Olivier 2005; Fadiga et al. 1995; Naish et al. 2014). Instead, sICI and ICF have rarely been used to investigate AON activity (Koch et al. 2010; Strafella and Paus 2000; Borgomaneri, Vitale, and Avenanti 2017), in particular during erroneous actions observation. They differ from the spTMS because they reflect the behavior of distinct populations of inhibitory and excitatory cortical interneurons without affecting spinal circuits (Kujirai et al. 1993). ICF and sICI may reflect the balance between excitation and inhibition mainly mediated by glutamatergic facilitation through N-methyl-D-aspartate (NMDA) receptors (Ziemann et al. 2004; Nakamura et al. 1997) and GABA-ergic inhibition through GABA receptors (Di Lazzaro et al. 2000; Ilić et al. 2002; Tandonnet, Garry, and Summers 2010; Ziemann et al. 1996). Action stimuli consisted in knotting actions. While observing someone tying a knot, procedural errors are often conveyed by small visual cues, i.e. the rope passing top-down instead of bottom-up, which however, are very important as far as goal achievement is concerned. Interestingly, the use of knots tying, instead of others goal-directed action, reduces the possibility that subjects resort to inner verbalization to rehearse the sequence (Balconi and Caldiroli 2011; Sitnikova et al. 2008; Võ and Wolfe 2013; Maffongelli et al. 2015). Knots are indeed very hard to describe verbally, and the didactics of knots is almost never based on textual (books) or spoken (online tutorials) material, but rather on visual demonstrations. We used two different type of errors, procedural errors (wrong passage of the rope) and control errors (in which the rope suddenly appears cut in two segments, see Figure 11). Considering the direction of the TMS-evoked modulations, two alternative predictions are possible

from: (1) the AON account (Bond et al. 1992; Frank and Ekman 1997; Sebanz and Shiffrar 2009) or (2) the predictive coding account (Friston 2005; Friston, Harrison, and Penny 2003; Friston, Mattout, and Kilner 2011). The first one suggests an important anatomo-functional overlap between action execution and observation. Following this analogy, increase of inhibition/reduction of facilitation are usually observed in both, volitional inhibition (Hoshiyama et al. 1996; Leocani et al. 2000; Coxon, Stinear, and Byblow 2006) and action error execution (Neubert et al. 2011; Reynolds and Ashby 1999). Based on the assumption that a strong overlap exists between these two mechanisms8, we should see the same pattern of results during the observation of an action misstep (increased inhibition and decreased facilitation). The second one suggests instead that action observation involves the minimization of the sensory prediction error (i.e., Bayesian-like inferences are generated and dynamically compared to the incoming sensory information). These prediction errors propagate through recurrent interactions among the different levels of the cortical hierarchy involved in action perception. The predictive coding framework would then predict greater facilitation and less inhibition in the presence of larger prediction error, as it is the case for the observation an action misstep (decreased inhibition and increased facilitation). The relative balance between local cortical inhibition and facilitation can in principle disentangle which one of the two views is the most effective in explaining how action missteps are incorporated in the representation of other's action.

(b)   Material and Methods

Participants

Nineteen naïve volunteers (8 females; mean age 24 years, range 20–29) participated in the study. All subjects were right-handed, as assessed by the Edinburgh Handedness Inventory (Oldfield 1971). None of the participants reported neurological, psychiatric or other contraindications to TMS (Simone Rossi et al. 2009). They had normal or corrected-to-normal visual acuity in both eyes and were unaware of the purposes of the study. All of them gave informed consent before the experiment, which was approved by the Ethics Committee of the Ferrara University and conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki.

Stimuli

The visual stimuli consisted of sequences of eight pictures showing the different steps of an actor (1 male and 1 female) tying a knot (Figure 11B). All pictures had a uniform black background. Two different actors (1 male, 1 female) recorded from a first-person perspective, were performing two different types of knots. The actors either completed the knot (Correct condition) or did a mistake in executing it (Execution Error condition) by introducing the extremity of the rope inside the loop from

top-down instead of bottom-up. This mistake results in the dissolution of the knot and was shown in the fifth picture of the sequence (see Figure 11B). In the Control condition, we modified the same fifth picture frame by showing the rope cut in two segments (Figure 11B). This causes the impossibility to achieve the goal as well, but for intrinsic object properties and not for action-dependent factors. In all conditions (Correct, Execution Error, Control condition) the first four frames of each sequence were the same (corresponding to the loop forming, see Figure 11). Thus, the 3 conditions are perfectly identical until the 5th frame. This choice avoids any prediction from the subjects.
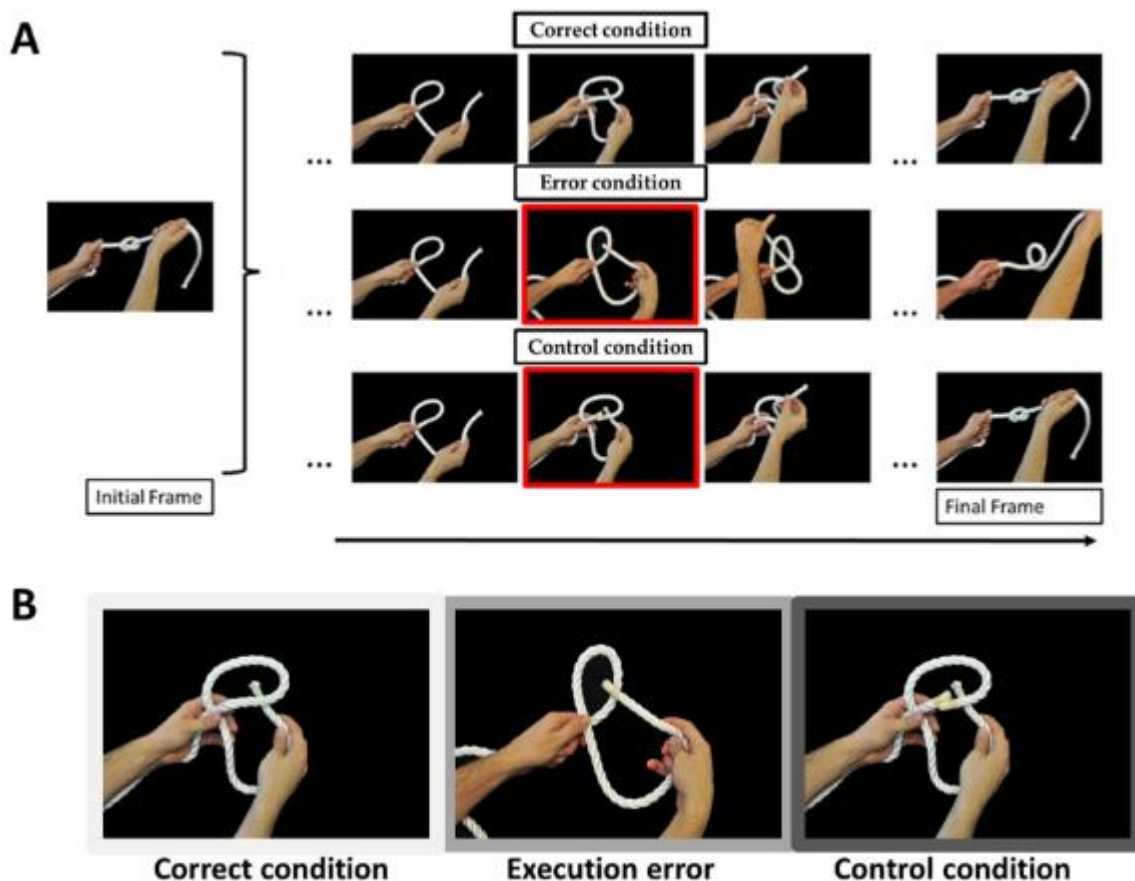
Figure 11: Stimuli and conditions.
In panel A, each row represents the timeline of the experimental conditions. For all conditions, the left part of the figure depicts the first frame shown (i.e. the expected final knot). The red squares highlight the frame associated to the error, in both Execution Error and Control conditions. In panel B, each picture shows, from left to right, the Correct, Execution Error and Control conditions.

TMS and electromyographic recordings.

Motor Evoked Potentials (MEP) were recorded with a wireless EMG system (Aurion, ZeroWire EMG) from the right First Dorsal Interosseus (FDI) muscle by using standard tendon-belly montage with Ag/AgCl electrodes. EMG traces were band-pass filtered (50–1000 Hz), digitized (2 kHz),

acquired by a CED power1401 board and visualized with Signal 3.09 software (Cambridge Electronic Design, Cambridge, UK). A 70 mm figure-of-eight coil connected to a Magstim BiStim stimulator (Magstim Co., Whitland, Dyfed, U.K.)

was placed over the left primary motor cortex with the handle pointing backwards at 45° from the midline. As optimum scalp position marked on the scalp of the subjects by using a make-up pencil, was considered the location on the scalp where maximum amplitude MEPs in the FDI were evoked at the lowest possible intensity (hot spot). The resting Motor Threshold (rMT) was assessed by using standard protocols (5 out of 10 MEPs exceeding 50 µV peak-to-peak amplitude67), with an inter-stimulus interval of ≅8 seconds. Three different stimulation protocols were used: Single pulse (spTMS), short interval Intracortical Inhibition (sICI) and Intracortical facilitation (ICF). During the spTMS protocol, a TMS pulse was delivered at the intensity of 120% of the rMT. During the paired-pulse TMS paradigm (ppTMS), sICI and ICF were assessed in accordance with an established protocol (Kujirai et al. 1993; Ziemann, Rothwell, and Ridding 1996). The intensity of the conditioning stimulus (CS) was set at 80% of the rMT. Before each experimental session we confirmed that this intensity never induced MEPs in 10 out of 10 repetitions. The test stimulus (TS) intensity was the same as that used in the spTMS session. In the ppTMS the inter-stimuli intervals (ISIs) of 3 ms and 12 ms were used to respectively assess sICI and ICF (Kujirai et al. 1993; Ziemann, Rothwell, and Ridding 1996; Borgomaneri et al. 2015).

Procedure and experimental design

Subjects were seated on a comfortable armchair. A 17" LCD computer monitor (1024x768 pixels; refresh rate: 60Hz) was placed at a distance of 58 cm from their frontal plane. Their right hand was placed on a cushion in a relaxed prone position. Before the experimental sessions, participants were familiarized with the visual stimuli. Each trial started with the presentation of a green central fixation cross displayed on a frame depicting the completed knot. After 2000 ms, the knot disappeared, and a sequence of pictures was shown. Each picture presentation lasted 200 ms followed by a delay of 800 ms TMS was administered after the fifth picture onset at 3 different delays: 120, 180 and 240 ms. Participants were instructed to look attentively at each picture sequence and to press a button when they detect something going wrong: wrong knot execution (execution error) or broken rope (control condition). In one third of trials (correct condition), participants did not have to produce any response. Responses were provided with the left hand, ipsilateral to the stimulated motor area, and were recorded by a custom-made response box. Reaction times (RTs) were collected relative to picture onset. In total, 270 trials were randomly presented to every subject: 3 experimental conditions (Correct, Control, Execution Error) X 3 stimulation protocols (spTMS, sICI, ICF) X 3 timings of stimulation (120 ms, 180 ms, 240 ms) X 10 repetitions. Twelve baseline trials for each stimulation

protocol (spTMS, sICI and ICF) were recorded at rest (eyes closed, subjects imagining a relaxing landscape70,71) at the beginning of the session, and at the end. The presentation of the stimuli, the timing of the TMS pulses and response collection were controlled by Psychtoolbox Version 3.0 (PTB-3), implemented in MATLAB (The MathWorks Inc., Natick, MA, USA).

Analysis

Behavioral data. Incorrect answers or RTs lower than 100 ms or higher than 1000 ms were discarded from the analysis (less than 7% of trials). RTs were analyzed by paired-samples two-tailed t-tests (significance threshold, $P < 0.05$). The same analysis was applied to responses accuracy.

Neurophysiological data. Preprocessing: Neurophysiological data were processed off-line by custom-made Signal script (Signal 3.09 software Cambridge Electronic Design, Cambridge, UK). As MEP amplitude we considered the peak-to-peak value (mV). MEPs associated with incorrect answers or with EMG activity in the 50 ms period prior to TMS were discarded from the analysis (less than 10% of total trials number). During spTMS and ppTMS, trials with MEPs lower than 0.05 mV were not considered as proper MEPs and were discarded (less than 2% of total trials number). The average number of trials in each condition was 9.5 trials ± 0.2.

Baseline modulation. In the first analysis our aim was to exclude modifications of intracortical and corticospinal excitability during the recording session. We compared baseline spTMS MEPs at the start and at the end of the experiment, with a two-tailed paired t-test. We also verified if sICI and ICF effects were in the direction of inhibition and facilitation, respectively. We ran a repeated-measures ANOVA on MEPs amplitude ratios between ppTMS protocols and the spTMS protocol (mean CS relative to mean TS)29,68, using the two protocols (sICI and ICF) and the two baselines as factors.

Generic action observation modulation. Furthermore, we verified wether the three TMS protocols were generically modulated by action observation (Fadiga et al. 1995). We compared baseline spTMS MEPs with pooled action observation conditions, with a two-tailed paired t-test. We ran a repeated-measures ANOVA on MEPs amplitude in the ppTMS protocols, using the two protocols (3 ms and 12 ms) and pooled action observation vs. baseline data as factors. As an additional check, we also verified that intracortical inhibition and facilitation was modulated by generic action observation (Strafella and Paus 2000; Patuzzo, Fiaschi, and Manganotti 2003). The ratio between ppTMS and spTMS was analyzed with a repeated-measures ANOVA using the two protocols (3 ms and 12 ms) and pooled action observation vs. baseline data as factors.

Error-related modulation. Finally, we evaluated the effect of the different action observation condition on intra-cortical and corticospinal excitability modulations. We used a within-subjects repeated-measures ANOVAs, separately for the spTMS and ppTMS protocols. In the spTMS protocol, the dependent variable was MEPs amplitude normalized by the average baseline. The

repeated-measures ANOVA included the factors Condition (Correct, Control, Execution Error) and Timing (120 ms, 180 ms, 240 ms). To quantify sICI and ICF action related effects, we expressed MEPs amplitude in the ppTMS sessions in function of the spTMS MEPs amplitude (Kujirai et al. 1993; Ziemann, Rothwell, and Ridding 1996; Borgomaneri, Vitale, and Avenanti 2015). For each experimental condition, we then computed a repeated-measures ANOVA using as index of intracortical modulation (iMEP) the mean ratio (ppTMScondition/spTMScondition) over the same mean ratio at baseline (ppTMSbaseline/ spTMSbaseline), separately for each ppTMS protocols (sICI, ICF). The relationship between the effect found in each condition was then transformed into percentages in multiplying by 100:

$$\left[\frac{(PP_{condition}/SP_{condition})}{(PP_{baseline}/SP_{baseline})} \right] * 100$$

A repeated-measures ANOVA was performed on these data with the within-subject factors TMS-protocol (sICI, ICF), Condition (Correct, Control, Execution Error) and Timing (120 ms, 180 ms, 240 ms). All analyses were run by using STATISTICA 9 (StatSoft, Inc.) using Newman-Keuls as post-hoc comparison ($P < 0.05$) and partial eta-squared for effect size.

(c)   Results

Behavioral data

Analysis on RTs did not show any significant difference between Execution Error (562 ± 70 ms, mean $\pm$ SD) and Control (551 ± 62 ms) conditions ($t(18) = 0.64$, $p = 0.52$). Similarly, the accuracy of the responses did not show any significant effect ($t(18) = 2.01$, $p = 0.06$) (Execution Error: 78 ± 16; Control: 86 ± 8).

Neurophysiological data

Baseline modulation. Baseline spTMS MEPs recorded at the beginning (mean raw MEP amplitude: 1.66 ± 1.2 mV), and at the end of the experiment (1.58 ± 1.3 mV) were not significantly different ($t(18) = 0.48$, $p = 0.63$), confirming no change of corticospinal excitability during the experiment (Chen et al. 1997). The 2×2 ANOVA between the TMS protocols (SICI, ICF) recorded in the two baselines (pre, post) revealed a main effect of protocols ($F(1,18) = 212,62$, $p < 0.001$; $\eta^2 p = 0.9$), with baseline sICI (mean CS/TS: 0.40 ± 0.36) significantly lower than ICF (1.30 ± 0.54). This result confirms that the two ppTMS protocols elicited the expected intracortical inhibition and facilitation in the baseline recordings. No other main effect ($F(1,18) = 0,29$, $p = 0.59$) or significant interaction

(F(1,18) = 2,56, p = 0.12) was found confirming no change of cortical modulation during the experimental sessions.

Generic action observation modulation

During generic action observation (all conditions together), spTMS MEPs amplitude (2.43 ± 1.44 mV) significantly increased compare to baseline (1.61 ± 1.21 mV; t(18) = 3.95, p < 0.001). This result suggests that generic action observation elicits a generic increase of corticospinal excitability, in agreement with previous reports (Fadiga et al. 1995). The ANOVA on MEPs amplitude during action observation and baseline in the two different protocols (ppTMS 3 ms: action observation: 2.98 ± 1.32 mV, baseline: 2.04 ± 1.13 mV; ppTMS 12 ms: action observation: 0.69 ± 0.73 mV, baseline: 1.11 ± 0.92 mV) showed a significant main effect of TMS-protocol (F(1,18) = 86.51, p < 0.01; η^2p = 0.82), with MEPs significantly smaller during the ppTMS 3 ms (mean MEP amplitude: 0.9 ± 0.8 mV) compared to ppTMS 12 ms (mean MEP amplitude: 2.5 ± 1.3 mV). A significant main effect of action observation was also observed (F(1,18) = 25.13, p < 0.01; η^2p = 0.58), with MEPs significantly smaller during the baseline (mean MEP amplitude: 1.37 ± 1.1 mV) compared to action observation (mean MEP amplitude: 2.04 ± 1.4 mV). The ANOVA revealed also a significant interaction between TMS-protocol and action observation (F(1,18) = 6.76, p = 0.01; η^2p = 0.2). Post hoc analyses evidenced higher MEPs amplitude in the ppTMS 12 ms protocol during action observation compared to other conditions (p < 0.01). In addition, amplitude of MEPs collected during the ppTMS 12 ms baseline was higher than in the ppTMS 3 ms protocols in both conditions (p < 0.01). Similarly to ppTMS 12 ms, MEPs amplitude for the two conditions were significantly different from each other in ppTMS 3 ms (p < 0.01). The ANOVA on intracortical excitability modulations (ratio between ppTMS and spTMS) during generic action observation and baseline showed only a significant main effect of the protocol (F(1,18) = 153.87, p < 0.01; η^2p = 0.8) with higher values in ICF (1.41 ± 0.4) than sICI (0.45 ± 0.2). The action observation main effect was not significant (F(1,18) = 0.618, p = 0.44) nor the interaction (F(1,18) = 3.39, p = 0.08). Although the interaction effect is not significant a trend was reported and is qualitatively visible in the ppTMS/spTMS ratios (ICF: action observation: 1.33 ± 0.29, baseline :1.49 ± 0.54; sICI: action observation: 0.48 ± 0.28, baseline: 0.42 ± 0.28).

Error-related modulation

The 3 × 3 ANOVA on spTMS between the condition and TMS timing revealed no significant interaction or main effects (all F < 1.20, p > 0.31) showing no specific modulation of corticospinal excitability induced by error observation. The 2 × 3 × 3 repeated-measures ANOVA on the intracortical modulation index showed a significant main effect of TMS-protocol (F(1,18) = 9,1051, p < 0.01; η^2p = 0.3), with iMEPs significantly smaller during the ICF (mean iMEP amplitude: 97% ±

31) compared to sICI (mean iMEP amplitude: 125% ± 48). Moreover, a significant 3-way interaction between TMS-protocol (sICI and ICF), Condition (Normal, Control, Error) and Timing (120, 180, 240) was observed ($F(4, 72) = 4,8966$, $p < 0.01$; $\eta^2 p = 0.2$). Post hoc analyses revealed a modulation of iMEPs in the sICI protocol only (Figure 12). Specifically, iMEPs recorded during the Execution Error were higher at 120 ms (142% ± 51) than in the other timings (180 ms: 122% ± 31, $p = 0.010$; 240 ms: 119% ± 42, $p = 0.009$). Moreover, at 120 ms iMEPs recorded during the Execution Error had higher amplitude than the Control and Correct conditions (Correct: 116% ± 42, $p = 0.006$; Control: 122% ± 46 SD, $p = 0.012$). A similar effect was found for the Control condition but at different Timing. The iMEPs values for the Control condition are higher at 240 ms (146% ± 69) compared to other Timing (120 ms: 122% ± 46, $p = 0.003$; 180 ms: 116% ± 45, $p < 0.001$). At this timing (240 ms), Control iMEPs had higher amplitude than the Correct and Execution Error conditions (Correct: 126% ± 48, $p = 0.010$; Execution Error: 119% ± 42, $p = 0.001$). No other main effect or interaction was significant. Summing up, these results point out a significant reduction of intracortical inhibition at 120 ms for the Execution Error and at 240 ms for the Control conditions (Figure 12).
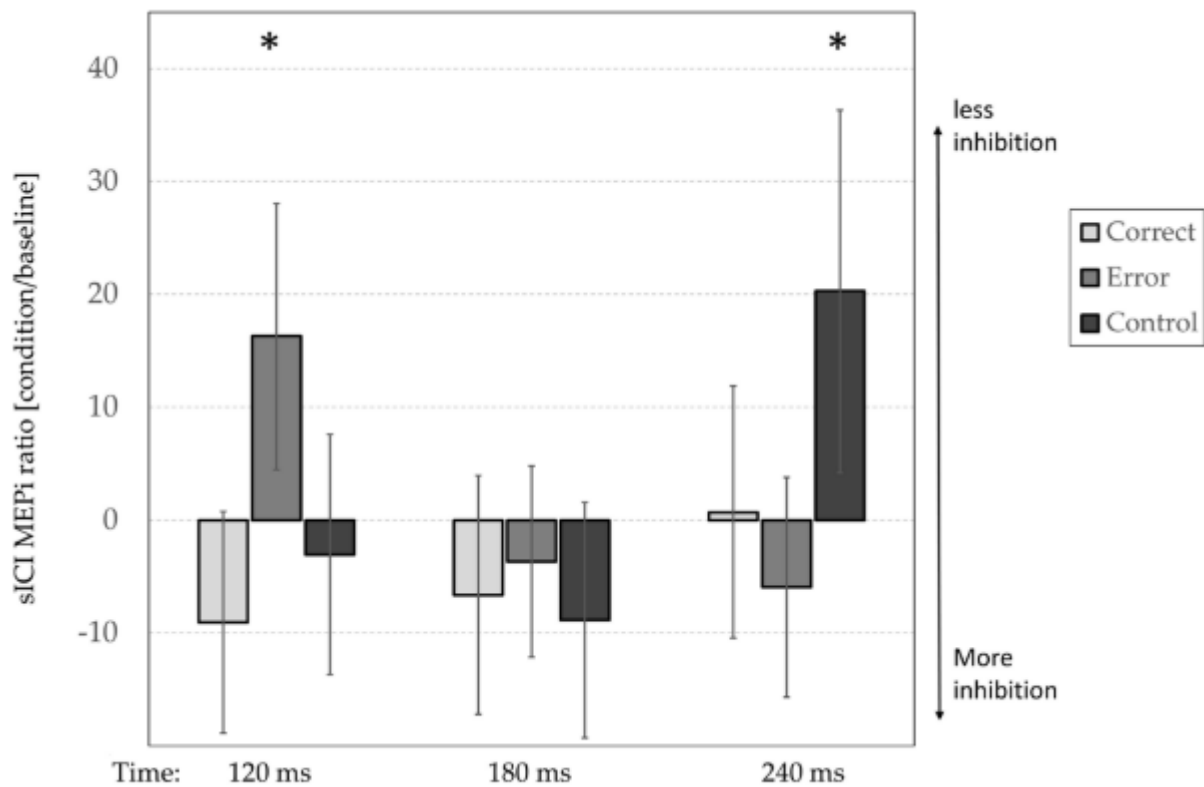
Figure 12: Intracortical inhibition results.
Modulation of the iMEP index (ratio of sICI in baseline and conditions, in function of the timing of the ppTMS (120, 180 and 240) in the three experimental conditions (see legend). Vertical whiskers, SEM. Asterisks indicate the significant comparison (Newman-Keuls, P < 0.05). To facilitate the understanding, data presented in this figure are normalized with respect to the mean.

(d)   Discussions

Action understanding is the building block of many important social cognitive skills, such as communication, imitation, intention understanding, learning and empathy (Blake and Shiffrar 2007). The relevance of predicting the consequence of other's actions to understand "what" is happening has been extensively discussed at a theoretical level (Summerfield et al. 2009). However, less is known about the neural mechanisms used to cope with the rather frequent circumstances where these predictions are wrong because an error happens in the observed action. In this study, we aimed at investigating whether and how the motor system is sensitive to the observation of action missteps. We demonstrated an early (120 ms) reduction of inhibition for the observation of a motor execution error, while the control error elicited a similar effect but with a longer latency (240 ms). A similar biphasic modulation has also been shown for corticospinal excitability during action observation (Barchiesi and Cattaneo 2013). In Barchiesi and Cattaneo (2013), the early corticospinal modulation followed the automatic mapping between action execution and observation properties, whereas later effects were driven by the recent history of visuomotor associative learning. In general, our results support the hypothesis that early and late motor activations induced by action observation may reflect two distinct mechanisms. Our early effect is associated to the presentation of a motor execution error. A delay of 120 ms was shown to be enough to activate the motor system during graspable object presentation (Franca et al. 2012). This condition requires that the observer maps the functional relationships between hands and rope positions to derive the presence of an error. The late effect instead, is triggered by a cut in the rope which, independently from the action performed by the actor, do not allow the successful conclusion of the action. The detection of this latter deviation from the expected action outcome, may require access to strategic and abstract reasoning regarding the feasibility of the action plan, that only later translates into the intracortical modulation of the motor cortex (Andersen and Cui 2009). Interestingly, using single and paired-pulse TMS protocols, we could investigate changes in corticospinal excitability as well as intracortical facilitatory (ICF) and inhibitory (sICI) circuits while participants were being presented with different types of errors. Notably, these indexes have already proven to be more sensitive than the MEPs recording during spTMS in detecting weaker sensorimotor associations (D'Ausilio et al. 2006). Corticospinal excitability reflects the effect of inhibitory and excitatory inputs to the descending corticospinal pathway. The sICI and ICF reflect distinct neurophysiological mechanisms (Ziemann et al. 2004; Liepert et al. 1998). sICI is associated to the activation of low threshold inhibitory interneurons in M1 mediated by gamma-aminobutyric acid (GABAa) receptors (Di Lazzaro et al. 2000; Ilić et al.

2002; Ziemann et al. 1996). The ICF more likely reflects the work of glutamatergic excitatory M1 circuits involving N-methyl-D-aspartate (NMDA) receptors (Ziemann et al. 2004). ICF, but not sICI, is thought to be influenced by the activation of long-range connections originating from remote brain regions (Ziemann et al. 2004; Ziemann 2004). Hence, our results reveal an early modulation of GABA-ergic inhibition in the motor system, driven by action error observation. Effects were observed for sICI but not for ICF, suggesting that the neural mechanisms involved in detecting action execution errors mainly consist in the modulation of intracortical inhibitory circuits. The lack of ICF effects is in line with previous studies showing no agreement on ICF modulations during action observation (Strafella and Paus 2000; Patuzzo, Fiaschi, and Manganotti 2003; Arias et al. 2014; Murakami, Restle, and Ziemann 2011). Similarly, previous works show that volitional inhibition in action execution does not affect ICF measures, but only sICI (Sohn, Wiltz, and Hallett 2002). Moving to the functional meaning of our results, according to the standard AON account, observing an action causes the reactivation of the same motor circuits in the observer's brain (Rizzolatti and Sinigaglia 2016). However, our results seem to go in an opposite direction. In fact, peri-movement modulation of sICI is associated to the mechanism by which voluntary movement is gated on and off. Indeed, the magnitude of sICI is reduced just before voluntary contraction (Reynolds and Ashby 1999), increased before its cessation (Buccolieri, Abbruzzese, and Rothwell 2004) and is somatotopically specific (Stinear and Byblow 2003). TMS studies of action observation have shown an increase of excitation in terms of corticospinal excitability (Fadiga et al. 1995) paralleled by a decrease in sICI (Strafella and Paus 2000; Patuzzo, Fiaschi, and Manganotti 2003). These findings parallel the local intracortical excitatory and inhibitory dynamics observed during actual action execution by shifting the balance towards greater local excitation (Strafella and Paus 2000; Patuzzo, Fiaschi, and Manganotti 2003). As a consequence, observing action errors would set in motion the neural cascade of events that normally occur during the suppression of erroneous voluntary movements. For instance, in the stop-signal task a decrease in corticospinal excitability and an increase of sICI (Hoshiyama et al. 1996; Coxon, Stinear, and Byblow 2006) is commonly observed. The magnitude of sICI acting on the agonist muscle increases also in the No-Go phase of a Go/No Go reaction time task (Sohn, Wiltz, and Hallett 2002), and in a countermanded reaction time task when the prepared movement is successfully retained (Coxon, Stinear, and Byblow 2006). This sICI increase was also present in others muscles, not engaged in the action (Hammond and Vallence 2007) and may prevent unwanted activations (Liepert et al. 1998; Sohn, Wiltz, and Hallett 2002). Our results, however, show that when an action error is detected, a decrease in inhibition rather than an increase is present. This is the opposite of what we would expect from a complete functional match between action execution and action observation processes. The predictive coding account (Friston 2005; Friston, Harrison, and Penny

2003), which has also been extended to explain mirror-like activities (Kilner and Frith 2007; Kilner, Friston, and Frith 2007), could offer some insight. This model suggests that the brain uses all available information to continuously predict forthcoming events and reduce sensory uncertainty by dynamically formulating perceptual hypotheses (Donnarumma et al. 2017). The formulation of perceptual hypotheses and their verification against incoming data, is fundamentally constrained by knowledge about the neural and biomechanical organization of movements (D'Ausilio, Bartoli, and Maffongelli 2015a; Donnarumma, Dindo, and Pezzulo 2017). This process occurs at all levels of the cortical processing hierarchy and is hypothetically instantiated in two types of computational units (Summerfield et al. 2009; Summerfield et al. 2006), representation and error units. While the representation units encode the predictions based on prior information, the error units compare the incoming signals with the predictions conveyed via the representation units. The discrepancies between predictions and input signals generate a prediction error signal. This prediction error signal updates the generative model at the next level of the cortical hierarchy and is consequently a critical component of the predictive mechanism (Summerfield et al. 2009; Friston 2010a). In this context, the main function carried out by the AON could be that of computing prediction errors based on visually perceived actions and to propagate them throughout the motor hierarchy (Aglioti et al. 2008; Urgen and Miller 2015; Kilner et al. 2004; Vastano et al. 2016; Wilson and Knoblich 2005; Urgesi et al. 2010; Costantini et al. 2014). Therefore, greater AON activities should correspond to either greater prediction errors or errors whose implications extend across the motor hierarchy. Remarkably, our study significantly expands on these aspects by showing that observing erroneous actions does not elicit increased inhibition as it would be predicted by the classic view about motor mirroring of other's action. Instead, the release from inhibition could be explained by the greater mismatch with respect to the generated top-down predictions. Action errors, as the one we investigated here, provide relatively small visual cues to disentangles errors from correct events. Nevertheless, these visual cues contain significant informative messages since the implications of such small and local differences directly propagate throughout the action hierarchy making it readily clear that the action goal will not be achieved.

Part 2. Joint Action

1. **Study 1: Predicting the postural adjustments during reach-to-grasp action by oneself or interacting dyads.**

It is recurrently claimed that human effortlessly detect others' hidden mental state by simply observing their movements and transforming the visual input into motor knowledge to predict their behavior. Using a classical paradigm quantifying motor prediction, we tested the role of vision during a reach and load-lifting task performed either alone, or with the help of a partner. Wrist flexor and extensors muscle activities were recorded on the supporting hand. Early muscle changes preventing limb instabilities when participants performed the task by themselves, revealed the contribution of the visual input in postural anticipation. When the partner performed the unloading, a condition mimicking a split-brain situation, motor prediction followed a premature pattern evolving along the task course and gaining from the integration of the successive somatosensory feedbacks. Our findings demonstrate that during social behavior, further to self-motor representations, individuals adapt the cooperation by continuously integrating sensory signals coming from various sources.

My Contribution: protocol definition, data analysis, results interpretation and manuscript writing

This work is currently submitted in Cerebral Cortex:

A Campos, PM Hilt*, L Fadiga, C Veronesi, A D'Ausilio and T Pozzo. Predicting the postural adjustments during reach-to-grasp action by oneself or interacting dyads.

Imagine a waiter lifting with his right hand a glass of wine on a plate he is holding with the left hand. The success of such bimanual asymmetric task depends on the waiter capacity to counteract the upward perturbation induced by the unloading movement. In such a context, the central nervous system can anticipate movement consequences and produce anticipatory postural adjustments (APAs; Hugon, Massion, and Wiesendanger 1982; Massion et al. 1999). APAs consists in using an efference copy (Wolpert 1997) of the motor command descending toward the lifting hand to prevent the disturbance exerted on the postural hand.

When the two hands hold the plate and the glass, APAs on the postural hand start before the onset of the unloading action. If a reaching phase precedes the unloading action, APAs could integrate the efferent copy to the visual feedback on the reaching and optimize the two hands coordination. Whilst interesting, previous investigations did not provide the appropriate experimental context to understand how these two signals contribute to efficient bimanual interactions. Indeed, either participants bimanually picked up objects with the two hands already positioned on the recording set up (Hugon, Massion, and Wiesendanger 1982; Dufossé, Hugon, and Massion 1985; Viallet et al. 1992; Barlaam et al. 2011) or initiated the unloading by pressing a button (Diedrichsen et al. 2003). Further, when a reaching movement was included, the task was performed without visual feedback (Ng et al. 2013).

The first goal of this study was to investigate the role of the visual feedback in the genesis of APAs by introducing a reaching phase preceding the bimanual load-lifting phase. Since one of the key tenets of APAs is that they must be self-produced (Diedrichsen et al. 2003), we should find APAs independently of visual feedback, and the task performed with eyes open or closed, should in principle produce identical results.

The investigation of how vision can impact on APAs may be essential if we extend the scope to the joint action scenario (Sebanz, Bekkering, and Knoblich 2006) where the waiter offers the glass to a guest. While APAs remain essential to the effectiveness of the dyadic interaction, the sole predictive signal is now provided by the visual cues about the guest's hand trajectory toward the glass. In the next step of the current study, we seek to verify if residual APAs, in the joint action condition, might be driven by visual cues even in the absence of any efference copy signal. APAs are predicted on the fact that action observation elicits subthreshold sensorimotor activations analogous to those recruited during action execution (Fadiga et al. 1995; Rizzolatti and Sinigaglia 2016). Importantly, this sensorimotor recruitment has already shown some degree of anticipation with respect to the ongoing observed action (Borroni et al. 2005) and has been proposed to be a key asset in allowing others'

action prediction both in absence of any interaction (Avenanti et al. 2013) and during joint action conditions (Pezzulo et al. 2017).

(b)   Materials and Methods

Participants

Seventeen couples of individuals took part in the experiment (8 man-man and 9 woman-woman; mean age: 25.5±2.5 SD). All participants had normal sensorimotor abilities and did not present any neurological or psychiatric disorders. No explicit information was given about the purpose of the study before the experiment. All participants gave informed consent to participate to the experiment. Procedures were approved by the local Ethics Committee and were fully complying with the Declaration of Helsinki.

Experimental procedure

The two participants sat comfortably on two chairs positioned face-to-face separated by a table (dimension: 1 x 0.3 m; Figure 13). In each couple, one participant was designated as the "Carrier", the second as the "Partner". Roles were kept the same during the whole experiment. The carrier role was to hold stable an object positioned on his left hand, until this object was lifted. The object was a touch-sensitive cylinder weighting 300g (6 x 18cm; diameter x height). The carrier held the object on a flat tray fixed to his hand by means of a Velcro strap. The tray was made of two platforms spaced 3cm (dimension: 10 x 10 the top wood, and 7 x 7 cm the bottom one) to fit four load cells between them. The left arm of the carrier was kept flexed on the table with the wrist supinated and fingers pointing forward in an unconstrained posture throughout the entire experiment session. In a first experimental condition, the partner had to reach, grasp and lift the carrier's object with his right hand (Joint condition; Figure 13B). In a second experimental condition, the carrier performed the same task by her/himself (Self condition; Figure 13A) by holding the tray with his left hand while reaching, grasping and lifting the object with her/his right hand. These two conditions were carried out with the carrier having either the eyes opened (EO) or closed (EC). In all conditions, reaching movement onset was self-paced and detected by a touch sensor fixed on a square plate (side: 10cm), marking on the table the starting position of partner's right hand.
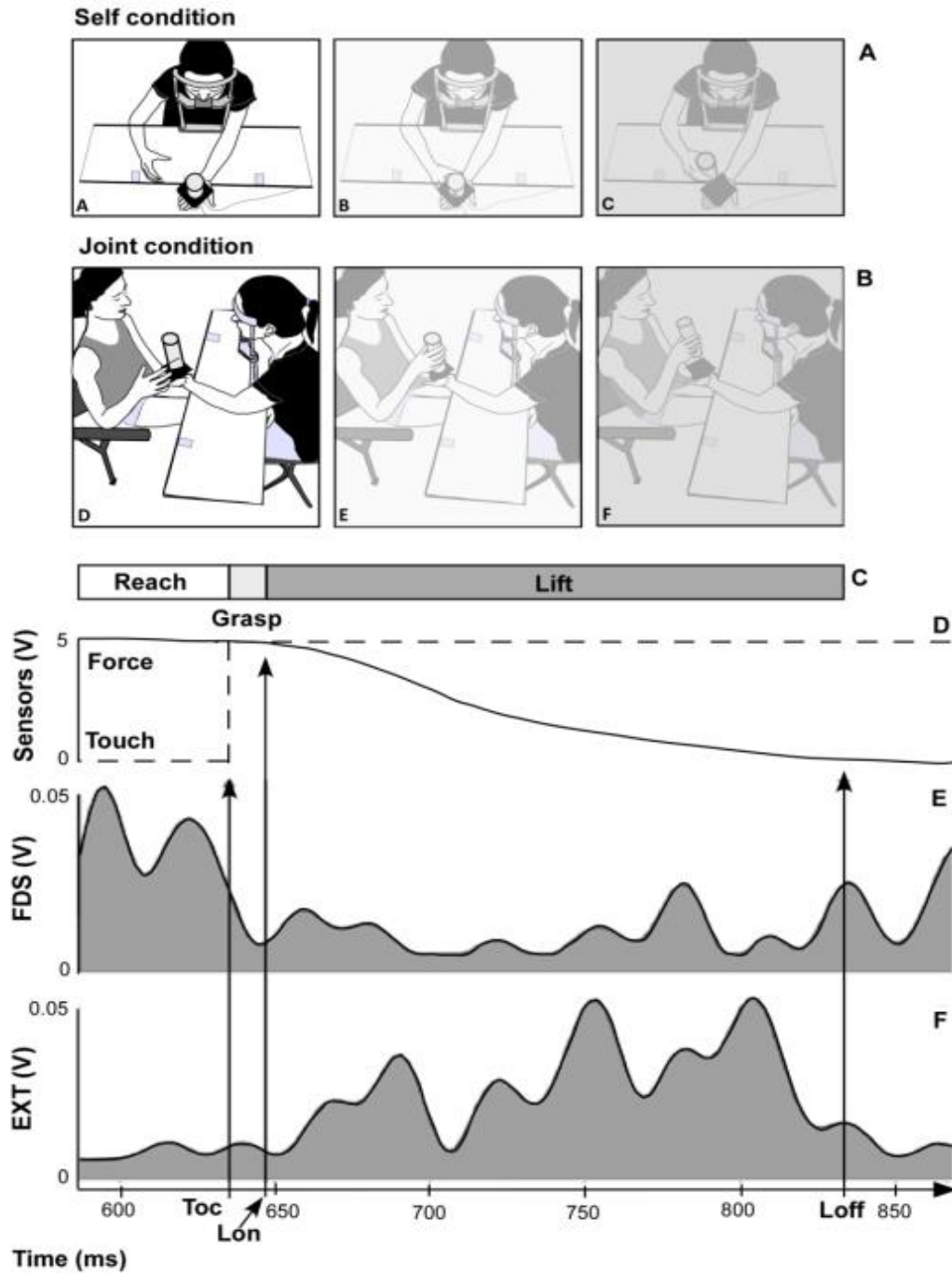
Figure 13: Experimental setup.
(A) Self condition: frontal view of the carrier holding the object with his left hand and reaching (left), grasping (middle) and lifting (right) the object with his right hand. (B) Joint condition: Lateral view of the carrier (black dress) holding the object with his left hand, while his partner (grey dress) reach (left), grasp (middle) and lift (right) with his right hand. In all experimental conditions, the carrier had to keep his left arm flexed on the table with the wrist supinated holding the object in his hand. The bar situated below the pictures (C) represents the duration of the different phases of the task: reaching (white), grasping (light gray), lifting (dark gray) for a typical trial (condition self-EO). These phases were determined based on touch and load sensors displayed below (D). The two lower panels show the muscle activity of wrist flexor (FDS; E) and extensor (EXT; F) muscles for the same trial. Vertical lines indicate the moment at which the object was touched (Toc), at which the lifting of the object started (Lon) and at which the lifting ended (Loff).

The combination of these experimental conditions allowed us to evaluate the respective influence of somatic, visual and efference copy signals on an agent capability to anticipate the object lifting (Figure 14). In fact, to verify the effect of integrating somatic and visual inputs with the efferent signal on APAs, three movement phases were identified, each reflecting the presence of different combinations of predictive signals. These phases are respectively aligned to the onset of finger touch with the object (Toc for time of contact), Lift onset (Lon) and Lift offset (Loff). As illustrated in Figure 14, visual feedback (Vfb) and efference copy are progressively integrated by touch feedback (Tfb) and force feedback (Ffb) during Self-EO condition, while Self-EC instead lacks Vfb. Joint-EO closely matches the information present in Self-EO though lacking the critical contribution of efference copy. Finally, the Joint-EC lacks both Vfb and efference copy, while keeping only Tfb and Ffb. The experiment was run in two randomized blocks for each experimental condition: self-EO, self-EC, Joint-EO, Joint-EC. Each block consisted in 20 trials and was followed by 5 min of rest. During rest periods, instructions concerning the upcoming block were given. Before starting the recording, a variable number of training trials (~ 8 trials with EO and EC in both conditions) were run until the participants felt confident with the task. The entire procedure lasted around 40 min.
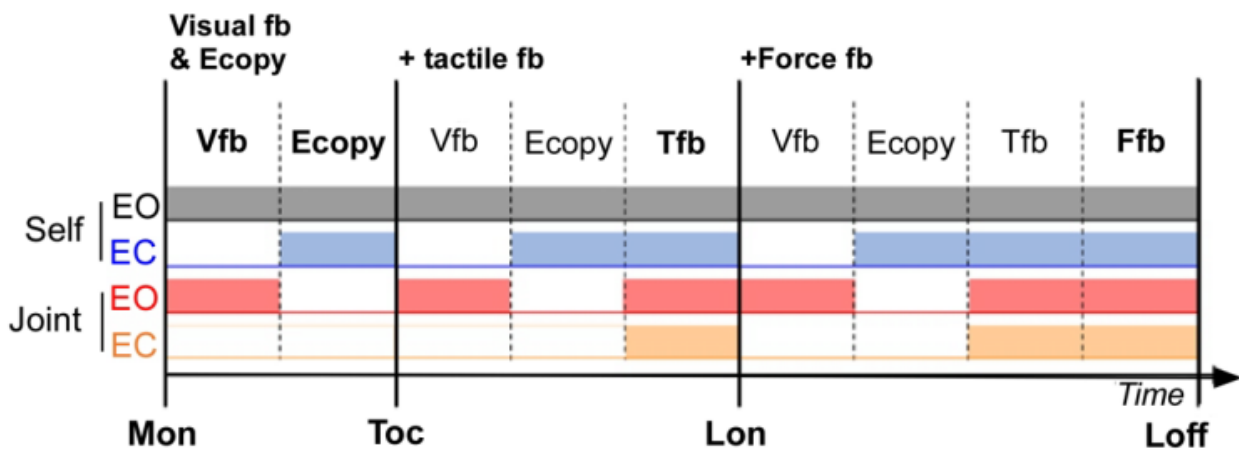
Figure 14: Illustration of available sensorial information at each phase of the task.
General schema showing the signals available for prediction in each phase of task: reaching, grasping and lifting. Start: for reaching movement onset (Mon); Touch: time of hand contact with the object (Toc); lift onset (Lon), lift offset (Loff). Shades of grey, blue, red and orange represent available information in each phase for experimental conditions. Self when the task was performed alone, and joint when it was performed by dyads. Eyes opened (EO) and closed (EC), Efference copy (ECopy), visual, tactile or force feedback (Vfb, Tfb, Ffb, respectively) become progressively available during the task.

Electromyographic and Behavioral Signal Acquisition

All data were acquired via an acquisition board (CED Power1401-3A, Cambridge Electronic Design, Cambridge, UK) and stored on a PC with Dasylab Software (MCC corporate, Norton, USA).

The electromyographic signal was recorded using a wireless system (Aurion, Italy) amplifying the data (gain of 1,000) and digitizing at 2000 Hz. Electrodes were arranged according to a bipolar tendon-belly montage over the flexor digitorium superficialis (FDS; Figure 13E) and the extensor digitorium communis (EXT; Figure 13F) of the carrier's left arm for all conditions. Three other types of behavioral data were simultaneously acquired: (1) touch signal coming from the right hand starting place (binary signal: value 5 if the hand is in contact with the starting place, value 0 from the start of the reaching movement); (2) touch signal coming from the object holding by the Carrier (binary signal: value 5 when the hand is in contact with the object, value 0 before the grasp of the bottle by the right hand; Figure 13D); and (3) weight-related signal coming from the four load cells situated in the tray (continuous signal; Figure 13D). These signals were recorded to define the movement phases and the precise events of object release from the tray supported by the carriers.

Data Analysis

Definition of movement phases: The right-hand movement onset (Mon) was determined as the first point at which the touch signal coming from the starting place reached a null value (for a minimum of 50ms). The right-hand time of contact with the object (Toc) was determined as the first point at which the touch signal coming from object reach a value of 5 (for a minimum of 50ms; Figure 13). The beginning and the end of the lifting phase (respectively Lon and Loff) were extracted from the tray's load signal. Lon was defined as the first time-point dropping below 95% of the maximal load value (for a minimal duration of 50 ms). Loff was defined as the first time-point dropping below 5% of the maximal load value (for a minimal duration of 50 ms). By using these time-points, the duration of each movement phase was computed (Figure 13C): (1) Trial duration – from Mon to Loff; (2) reaching duration – from Mon to Toc; (3) grasping duration – from Toc to Lon, (4) lifting duration – from Lon to Loff.

EMG processing: EMG signals of each muscle were first visually inspected trial-by-trial to control for the presence of recording artefacts. No trial was discarded after this procedure. FDS and EXT EMGs for each trial were first high-pass filtered (20 Hz) and then digitally full-wave rectified and low-pass filtered (Butterworth filter, cut-off frequency of 5 Hz, zero-phase distortion; Kubicki et al. 2016) and normalized to 1,000 time steps. Compared to the tonic activity enabling the maintenance of the object on the tray, the unloading is compensated via a decrease of FDS activity and an increase of EXT (Figure 13E and F). To evaluate these modulations, EMG signals were cut and temporally aligned to Toc (from Toc-500ms to Toc+1000ms), Lon (from Lon-500ms to Lon+1000ms), and Loff (from Loff-650ms to Loff+850ms) for each trial. For each alignment, each participant and each experimental condition, we computed the mean activity of FDS and EXT muscles. We then evaluated the presence of EXT activations and FDS deactivations using a semi-automatic algorithm. For each

participant, we defined the onset of activation (EXT) or deactivation (FDS) as the first time-point at which muscle activity was higher (EXT) or lower (FDS) than the tonic baseline activity, for a minimum duration of 150ms. Baseline activity was computed for each participant and each muscle as the mean muscle activity on a 350ms window (from Toc-550ms to Toc-200m) adding (EXT) or subtracting (FDS) 3 standard deviations. Further, muscles adjustments were studied based on movement phases: reaching-APA (before Toc), grasping-APA (before Lon) and lifting-APA (before Loff).

Statistical Analysis

The Shapiro-Wilk test was used to check the normality assumption for parametric tests. Data were not all normally distributed ($p<0.05$). Thus, all statistical comparisons were done using two-tail permutation tests (5000 permutations; Matlab function mult_comp_perm_t1). All P-values were corrected for multiple comparisons using the Benjamini-Hochberg False Discovery Rate (Matlab function fdr_bh).

(c)   Results

Task Learning effects

The first analysis considered the difference between the two recording sessions of each condition to evaluate a potential learning effect. No significant difference was found between experimental blocks for the duration of each movement phases (Statistical analyses in Supplementary Material L). Also, APAs for both FDS and EXT aligned to Toc, Lon and Loff did not differ (Statistical analyses in Supplementary Material L). Thus, since no learning effect was visible, analyses were run on all trials. The absence of learning effects suggested that the task is a well-learned and automatic daily action. All numerical results presented in this part are expressed in mean ±SEM.

Movement phases Duration

The duration of the reach and grasp actions (all: Mon-Lon; reach: Mon-Toc; grasp: Toc-Lon) were significantly longer in the self-EC condition (all: 898±40ms, reach: 613±32ms, grasp: 81±12ms, respectively) compared to the three other conditions (self-EO: all=718±28ms, reach=534±26ms, grasp=13±4ms; Joint-EO: all=753±28ms, reach=523±20ms, grasp=33±9ms; Joint-EC: all=760±28ms, reach=527±19ms, grasp=32±7ms; $p<0.05$). Thus, reaching duration was comparable when performed by the partner or the carrier herself. This excluded any mechanical effect due to potential higher hand momentum on the consecutive grasping and unloading phases and makes possible a suitable comparison of APAs between Self-EO and Joint-EO/EC conditions. Differently,

the duration of lifting phase (Lon-Loff) was shorter in self-EO (172±6ms) compared to other conditions (self-EC: 204±4ms; Joint-EO: 197±7ms; Joint-EC: 201±8ms; p<0.05). No other significant difference was found (Figure 15).
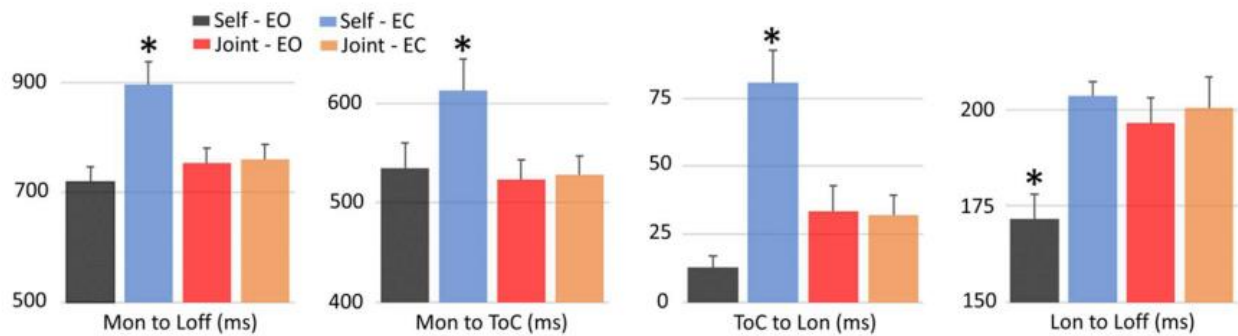
Figure 15: Movement phases durations.

Durations (in ms) of movement phases for each experimental condition. From left to right: (1) trial duration: from the onset of reaching movement (Mon) to the end of object lifting (Loff), (2) reaching duration: from Mon to the time of contact with the object (Toc), (3) grasping duration: from Toc to the onset of the object lifting (Lon), (4) lifting duration - from Lon to Loff. Asterisks indicate significant differences (p<0.05). Bars represent standard errors.

EMG activation/deactivation onset

Figure 16 shows the average FDS deactivation and EXT activation time-course with respect to each of the three identified time-points (Toc, Lon and Loff). Figure 17 instead represents the muscle activation (EXT) or deactivation (FDS) onset in relation to the three kinematic landmarks (Toc, Lon and Loff).
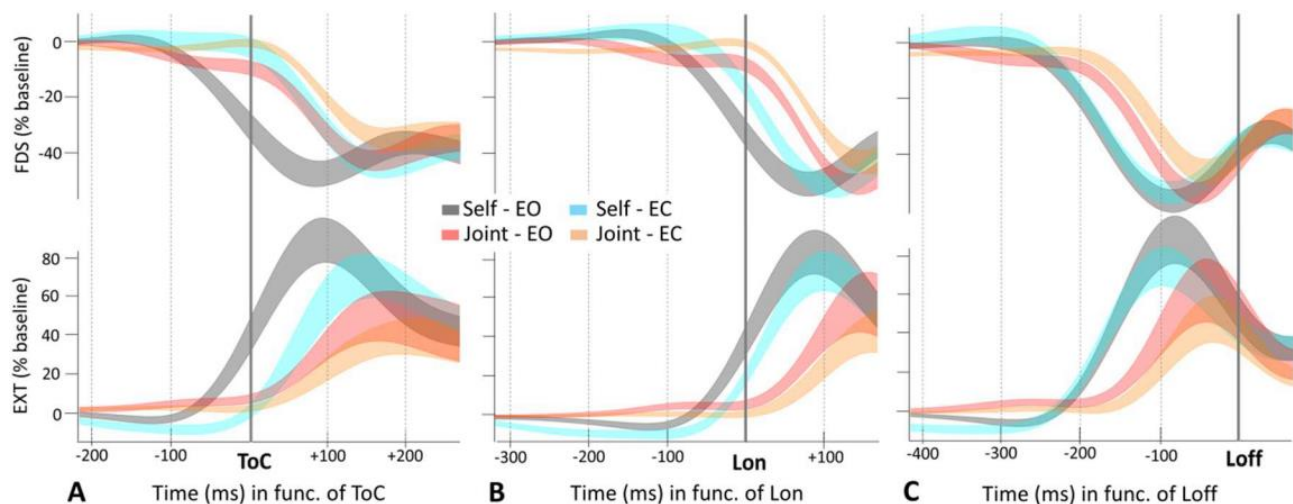
Figure 16: Electromyographic activation patterns.

Standard errors around the mean of electromyography activity of flexor (FDS, upper panels) and extensor (EXT, lower panels) muscles, aligned on time of contact with the object (Toc), lift onset

(Lon) and lift offset (Loff), for each experimental condition (Self-EO in grey, Self-EC in light blue, Joint-EO in red, Joint-EC in orange). EO, eyes opened; EC, eyes closed.

APA before time of contact: FDS onset deactivation appeared significantly sooner in the two EO-conditions (Self: -83±11ms; Joint: -45±22ms) compared to the two EC-conditions (Self: 20±19ms; Joint: 54±19ms; p<0.05). The activation of EXT in Self-EO condition occurred significantly earlier than in Self-EC (53±12ms; p<0.05, t=-9.1) and in Joint-EC (48±15ms; p<0.05, t=-4.6). No other significant difference was found (Figure 17A).

APA before lift onset: FDS deactivation in Self-EO (-85±9ms) occurred significantly sooner compared to the three other conditions (Self-EC: -23±25ms, p<0.05, t=-2.3; Joint-EO: -36±19ms, p<0.05, t=-2.3; Joint-EC: 48±15ms, p<0.05, t=-8.9). Inversely, FDS deactivation during Joint-EC was significantly later than the other conditions (Self-EC: p<0.05, t=-2.3; Joint-EO: p<0.05, t=-4.1). A similar pattern of results was found for EXT. Activation in Self-EO (-40±9ms) was significantly sooner than Joint-EC (29±13ms, p<0.05, t=-4.1), marginally different from Self-EC (-15±7ms, p=0.05, t=-2.4), but no different than Joint-EO (14±38ms). Additionally, EXT activation in Joint-EC was significantly later than in Self-EC (p<0.05, t=-3.6; Figure 17B).

APA before lift offset: There was no difference between Self-EO (FDS: -225±6ms; EXT: -206±8ms) and Self-EC (FDS: -214±8ms; EXT: -217±7ms) for both muscles. Further, the onset of activation for EXT and deactivation for FDS in the two Self conditions appeared significantly sooner compared to the two Joint conditions (Joint-EO: FDS: -183±7ms, EXT: -168±8ms; Joint-EC: FDS: -152±16ms, EXT: -140±14ms; p<0.05). In addition, a significant difference between the conditions Joint-EO and Joint-EC was found for EXT onset of activation (p<0.05, t=-1.8; Figure 17C).
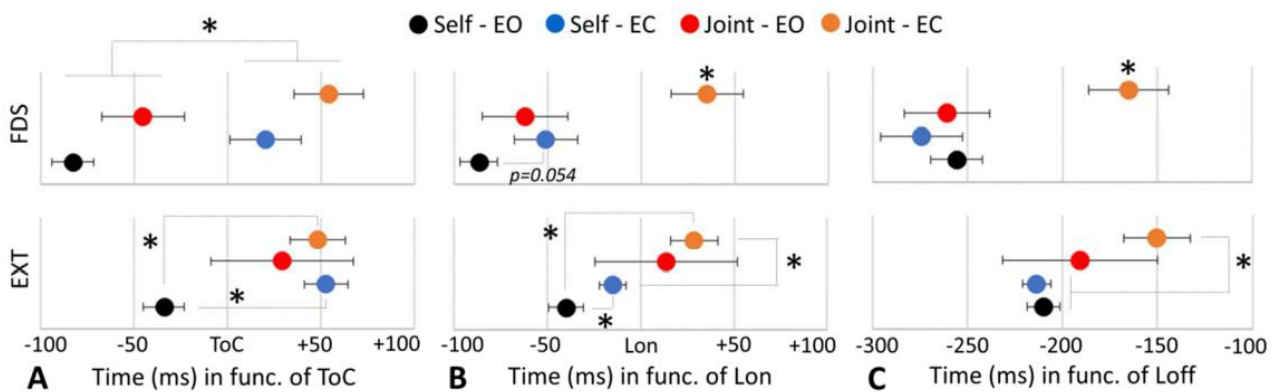
Figure 17: Activation and deactivation onset.
EMG flexor (FDS) deactivation and extensor (EXT) activation onset in function of the time to contact with the object (Toc, left panel, A), the lift onset (Lon, middle panel, B) and the lift off (Loff, right panel, C). Experimental conditions are Self-EO in grey, Self-EC in light blue, Joint-EO in red, Joint-EC in orange. EO, eyes opened; EC, eyes closed. Asterisks indicate significant differences (p<0.05).

To better interpret these results, Figure 18 illustrates the averaged onset of FDS deactivation and EXT activation in function of movement phases and experimental conditions. The figure highlights a clear effect of visual information on the timing of APAs. Indeed, delayed APAs are observed in the two EC conditions. In the Self-EC condition APAs started after Toc and the grasping duration also was also prolonged. The Joint-EC is the only condition in which APAs initiate after Lon. Finally, in Joint-EO the APAs compared to Self-EO is slightly shortened but still visible. However, as shown in Figure 16 the amplitude of FDS deactivation before Toc is far smaller during Joint-EO when compared to Self-EO, suggesting an incomplete anticipation when the efference copy is available.
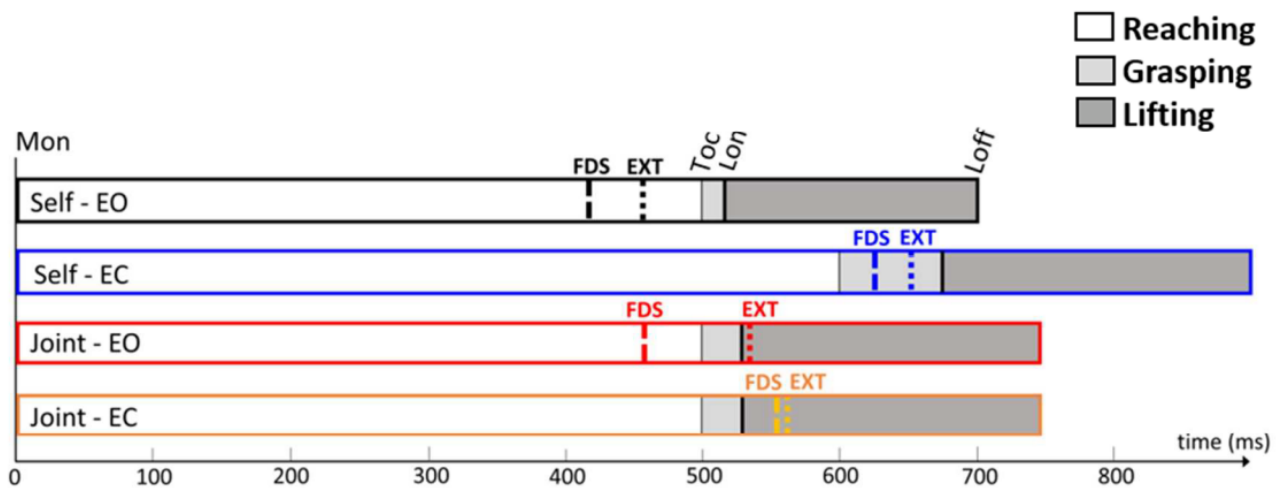
Figure 18: Main results illustration.
Illustration of the averaged onset of FDS deactivation and EXT activation in function of the different kinematic landmarks (Mon, Toc, Lon, Loff) and the four experimental conditions (black: Self-EO; blue: Self-EC; red: Joint-EO; orange: Joint-EC). Reaching phase from movement onset (Mon) to time of contact (Toc) in white, grasping from Toc to start of lifting (Lon) in light grey, and lifting from Lon to lift off (Loff) in dark grey.

(d)   Discussion

When participants performed the task themselves in full vision, muscle activities showed early APAs before the grasping onset. Without visual input, muscle changes on the load-bearing hand were significantly delayed after the grasping onset, similarly to the classical APAs (Hugon, Massion, and Wiesendanger 1982; Dufossé, Hugon, and Massion 1985; Massion et al. 1999). Importantly, APAs were present in the joint action scenario, though significantly modulated by the lack of efference copy signal and thus depended on accumulating sensory information.

The behavioral analysis revealed longer movement duration in Self-EC compared to EO condition, suggesting the crucial role of the visual feedback for the task achievement. In fact, all movement phases (reaching, grasping, and lifting) increased, the first slower reaching impacting successive

grasping and lifting durations. Herein, participants were asked to reach a big object requiring a rough cylindrical hand grasp. Thus, the longer reaching duration did not reflect an impairment to monitor the reaching without visual feedback and to update the internal representation of target location. Indeed, object size, shape and distance were compatible with a successful grasping without visual input (Gentilucci et al. 1997; Rand et al. 2007). The slower reaching thus rather reflected the difficulty to link the grasping with the lifting without vision. When performed by the partner, although reaching and grasping duration remained the same than in self, lifting phases was always longer compared to self-EO, providing the temporal condition for controlling the task in less predictive context.

APAs investigation revealed clear forearm muscle changes in the self with eyes open condition where flexor deactivation started about 100ms before the hand touched the object (reaching APA). This result is difficult to compare with previous investigations where the two hands systematically gripped on the object to be lifted (Hugon, Massion, and Wiesendanger 1982; Dufossé, Hugon, and Massion 1985; Barlaam et al. 2011) did not allow to verify the presence of APA during the reaching phase. However, such early-anticipated muscle modulation seems appropriate when the load-bearing hand is not mechanically stabilized, and consequently imposed huger spatial and temporal uncertainties to the reaching and grasping sub tasks. Oculomotor saccade toward the object to be grasped anticipating the hand reaching movement (Esposti et al. 2017) combined to the efference copy of the motor command could provide crucial inputs in producing reaching APAs. Without visual cues, flexor deactivation onset was systematically recorded after the grasping (grasping APA), suggesting that efference copy alone is not sufficient to generate reaching APAs.

Because APAs have not been observed when the unloading was generated externally (e.g., (Dufossé, Hugon, and Massion 1985; Aruin and Latash 1995), or when the perturbation was signalled by an auditory tone (Dufossé, Hugon, and Massion 1985; Witney, Goodbody, and Wolpert 1999) the presence of APAs in the dyadic context was unlikely. Anticipated muscle changes however followed a different pattern in joint condition compared to self-initiated APAs where the abrupt deactivation of the flexor muscle contrasted with the smooth change before touch followed by a sharp flexor deactivation recorded in Joint-EO. Smooth and early muscle changes could reflect pre-APAs, the benefit of which remaining however to be elucidated. Possibly, the visual cues would prepare APAs that will be later fully release when somatic inputs are available. One potential advantage would be to progressively integrate the sequence of sensory events expected along the task course (see Figure 14). The presence of flexor deactivation 150ms before the lift off when the efference copy and the visual feedback are lacking (Joint-EC condition), supports the contribution of the successive cutaneous and proprioceptive cues for ensuing late postural adjustments. Indeed, even delayed flexor

deactivation and extensor activation recorded before the lift off (lifting APAs) are compatibles with efficient postural adjustments. For instance, during a classical bimanual load-lifting task APAs are recorded about 30-20ms before the lift off (Hugon, Massion, and Wiesendanger 1982; Barlaam et al. 2011). The duration of the present haptic interactions (including the grasping and the lifting phases) is thus compatible with the timing of sensorimotor loops engaged in corrective actions (~100ms; Johansson and Flanagan 2009). A fast-cutaneous response (about 50ms, Cole and Abbs 1988) and a modulation of the flexor deactivation of the supporting hand (about 200ms before the Loff in Joint-EC) to assist the lifting movement are still possible when visual input and the efferent copy are lacking. Subsequently, longer grasping and lifting phases recorded in dyadic creates the temporal condition for a sensorimotor dialogue between the dyad, where the load bearing hand would assist the lifting hand. This agrees with the idea that APAs play a dynamic role in postural transition and provide additional force for the task goal achievement (Stapley et al. 1999; Hodges, Spatt, and Patterson 1999; Pozzo, Ouamer, and Gentil 2001).

Several causes could limit the predictions about the two agents' actions and thus promote a gradual sensorimotor integration to improve social interactions. Hand reaching movements, even if less variables when performed synchronously and without physical interaction (Sacheli et al. 2013), remains however strongly participant dependent and much less predictable than non-living object kinematic (Hilt et al. 2016; Berret et al. 2011). Further, self-bimanual movements represent a special case of multitasking requiring the organization of multiple command streams to control two effectors in addition to their temporal sequencing. Asking participants to perform the task with a pair (one agent picking with the right hand the object supported in by the left hand of the carrier) mimicks a 'split-brain' situation (Wiesendanger and Serrien 2004) where the corollary discharge of the motor command to the lifting hand can no more be relayed to subcortical structures that modulates the commands to the postural hand. Thus, a considerable amount of neural activity related to ipsilateral limb available in self-condition (Kermadi et al. 1997; Donchin, Cardoso de Oliveira, and Vaadia 1999) is missing in dyadic condition. Precisely, the basal ganglia (Wiesendanger et al. 1996) and the cerebellum (Nirkko et al. 1997) modulate hemispheric interactions during bimanual tasks. Investigations performed in patients with callosal lesion showed desynchronization of two interacting hands similarly in vision and no vision conditions. These results indicate the major role of the corpus callosum in exchanging sensory information about left and right limb motions and of the basal ganglia in adjusting the postural and the moving hand (Viallet et al. 1992; Serrien and Wiesendanger 2000). At last, previous artificial 'split-brain' experiment revealed that visual guidance alone was insufficient for perfect coordination of two independent arms (Perrig, Kazennikov, and Wiesendanger 1999).

Nonetheless, even if limited, visual cues about kinematic variables contribute to the dyadic interaction. Vision of others' actions has been demonstrated to recruit both the motor (Caetano, Jousmaki, and Hari 2007; Hari et al. 1998) and the somatic system (Avikainen, Forss, and Hari 2002; S. Rossi et al. 2002). These activations have been reported to anticipate the temporal deployment of observed actions (Rizzolatti and Sinigaglia 2016). These neurophysiological results fit with findings showing that the reuse of one's own bimanual model could have positive effects on the prediction of co-actor's action timing (Pezzulo et al. 2017). In our task, visual cues from partner's action might be used to anticipate the time of contact with the object and thus engage pre-APAs. However, visual perception of action and associated motor resonance partially support internal variables adjustment of two interacting agents. Rather, our findings demonstrate that during complementary actions (a common social behavior requiring flexibility), in addition to self-motor representations, individuals adapt a real time cooperation by continuously integrating sensory signals coming from various sources.

(e)   Additional data and analyses

L: Study 2.1: FDS/EXT onset of deactivation/activation

- FDS: Data (mean ±sem)

	ToC		Lon		Loff	
	Blok 1	**Blok 2**	**Blok 1**	**Blok 2**	**Blok 1**	**Blok 2**
Self-EO	-132 ±19	-152 ±29	-152 ±20	-170 ±21	-477 ±22	-493 ±27
Self-EC	78 ±58	32 ±38	-49 ±51	-108 ±60	-547 ±71	-513 ±62
Other-EO	-21 ±42	-25 ±45	-71 ±45	-101 ±41	-335 ±117	-484 ±40
Other-EC	239 ±86	136 ±51	201 ±88	63 ±43	-203 ±90	-325 ±52

- FDS: Statistics (permutation test): Blok 1 vs Blok 2

	ToC	Lon	Loff
Self-EO	p=0.74, t=0.50	p=0.67, t=0.62	p=0.67, t=0.45
Self-EC	p=0.74, t=0.47	p=0.67, t=0.46	p=0.67, t=-0.47
Other-EO	p=0.74, t=0.33	p=0.40, t=1.30	p=0.28, t=1.52
Other - EC	p=0.74, t=1.23	p=0.09, t=1.59	p=0.40, t=1.36

- EXT: Data (mean ±sem)

	ToC		Lon		Loff	
	Blok 1	**Blok 2**	**Blok 1**	**Blok 2**	**Blok 1**	**Blok 2**
Self-EO	-20 ±44	-66 ±22	-38 ±43	-87 ±25	-378 ±42	-425 ±23
Self-EC	97 ±21	41 ±39	-29 ±11	-113 ±46	-432 ±13	-515 ±46
Other-EO	84 ±96	67 ±58	38 ±100	24 ±66	-357 ±102	-377 ±62
Other-EC	216 ±86	150 ±66	187 ±86	136 ±78	-214 ±91	-259 ±69

- EXT: Statistics (permutation test): Blok 1 vs Blok 2

	ToC	Lon	Loff
Self-EO	p=0.51, t=1.21	p=0.59, t=1.21	p=0.60, t=1.16
Self-EC	p=0.51, t=1.39	p=0.58, t=1.71	p=0.60, t=1.69
Other-EO	p=0.94, t=0.28	p=0.86, t=0.25	p=0.90, t=0.22
Other - EC	p=0.80, t=0.64	p=0.86, t=0.51	p=0.90, t=0.44

2. Study 2: Multi-layer adaptation of group coordination to a sensorial perturbation

Human interaction requires mastering the integration of multimodal sources of information to achieve effective interpersonal coordination. The present study examines the movement-based interaction dynamics in an orchestra (one conductor and two sections of violinists), adapting to a perturbation affecting their normal pattern of sensorimotor communication (half a turn rotation of the first violinists' section). We explore the relation between different channels of communication (hand Vs. head kinematics) and the different modes of interaction (coordination versus synchronization). The instrumental movements (hand kinematics), highlighted robust leader to follower relations, substantially not affected by the experimental manipulation suggesting an important role of memory and score reading in this process. On the contrary, within ancillary movements (head kinematics), we could observe how the perturbation reshaped the social architecture of the orchestra. Indeed, the role of the second line of violinists evolved and, through a parallel regulation of inter-group coordination and intra-group synchronization, achieved status of mediator between the conductor and the first line. We show that complex, multi-agent, non-verbal interaction is achieved via the co-regulation of different modes of cooperation (complementary versus synchronous) through different channels of communication (ancillary versus instrumental movements) to flexibly adapt to contextual constraints.

My Contribution: data analysis, results interpretation and manuscript writing

This work is currently submitted in Scientific Reports:

PM Hilt, L Badino, A D'Ausilio, G Volpe, L Fadiga and A Camurri. Multi-layer adaptation of group coordination to a sensorial perturbation.

This work has been presented as a poster communication in the 17th international ACAPS congress (29th to 31st October 2017, Dijon, France):

PM Hilt, L Badino, A D'Ausilio, G Volpe, L Fadiga and A Camurri. Communication Dynamics in Orchestra: musicians-musicians and musicians-conductor

(a)   Introduction

Successful human-to-human interaction requires important behavioral adaptation, as well as prediction. A large body of literature has focused on cooperation towards shared goals, where humans must combine available sensory information with internal movement production models (Wolpert, Doya, and Kawato 2003; Sebanz and Knoblich 2009; Jeannerod 2001; Friston, Mattout, and Kilner 2011). In this regard, researchers investigated how dyads achieve interpersonal simple sensorimotor coordination, such as walking side-by-side (van Ulzen et al. 2008) or rocking in rocking-chairs (Richardson et al. 2007). In such contexts, co-actors continuously influence each other and tend to spatially and temporally synchronize their movements. Beside imitation, action complementarity play a key role in inter-individual coordination with the goal of achieving efficient collaboration (Newman-Norlund, Noordzij, et al. 2007). Social interaction indeed goes beyond synchronization with other's actions and relies also on inferring others' motor goals and intentions to generate a context-appropriate action. To achieve fast inter-individual coordination, individuals may build internal predictive models of other's behavior. In function of the context, the most appropriate motor model is compared with the current observed movement, to generate a prediction error (Friston, Mattout, and Kilner 2011) and update own motor planning (Sebanz, Bekkering, and Knoblich 2006). Due to the technical and analytical complexity in exploring the details of human sensorimotor interaction, only few experiments went further than a dyadic set-up (Fessler and Holbrook 2016; Dikker et al. 2017; Alderisio et al. 2016; Codrons et al. 2014). However, in daily life, things are usually much more complex. For instance, during a conversation, information is sampled through multiple channels (e.g. vision, audition), sometimes in parallel (e.g. information in the foreground and information from the background) and at different temporo-spatial scales (e.g. slow whole-body movements versus fast lip motions). At the same time, different kinds of information may be conveyed in parallel through different channels. For example, in speech, bodily gestures and spoken words are generally co-expressive (McNeill 2000). In this context, communication requires flexible means to integrate multimodal data, across multiple timescales and act accordingly. Therefore, proper quantification of (realistic) group coordination is today one of the key missing elements to understand how humans manage to interact with others by efficiently selecting, processing and sending information.

In this context, ensemble musicians have been proposed as an ideal model, by keeping the key multidimensional properties of natural sensorimotor interaction, but allowing relatively good experimental control (Volpe, D'Ausilio, et al. 2016; D'Ausilio, Novembre, et al. 2015). Few previous studies, by relying on kinematic recordings, have started to model sensorimotor information flows across musicians. D'Ausilio and collaborators (D'Ausilio et al. 2012) recorded violinists' and

conductors' movement kinematics to investigate causal relationships across musicians. They showed that conductors influenced communication between musicians and that aesthetic appreciation was dependent on the co-regulation of leader-to-musician and musician-to-musician communication patterns (D'Ausilio et al. 2012). Leadership in the orchestra scenario is explicit since the conductor determines tempo, selects musicians, leads rehearsals, and takes critical decision about interpretation of the pieces. In the absence of explicit leadership (e.g. quartet), this role is shared across musicians (Badino et al. 2014). The quartet scenario was also used by Chang and collaborators (Chang et al. 2017) to investigate the leader-follower relation during a manipulation of the visual information available to musicians: musicians faced 180 degrees away from the center (to prevent direct visual contact with each other). They showed that the influence of the leader on followers depended on visual contact, confirming that information flow is affected by a change in the available information. Beyond global descriptions of musician's pattern of relationships, the complexity of these kinds of scenario could also be exploited to distinguish and evaluate the existence of multiple channels of communication as well as their respective role in efficient coordination. In previous studies, one representative kinematic parameter was used to extract global coordination (D'Ausilio et al. 2012; Badino et al. 2014; Chang et al. 2017). However, we know that movements of different body parts may convey substantially different types of information. For instance arm movements in violinists directly control the sound output (i.e., instrumental gestures), whereas complementary torso oscillations may serve a secondary communicative purpose (ancillary gestures (Wanderley 2002; D'Ausilio, Novembre, et al. 2015)). More importantly, movements of different body parts may act as different channels of communication, possibly with different roles depending on the specific communication mode. For example, within a quartet (Badino et al. 2014; Chang et al. 2017), musicians have specific roles while in orchestras, musicians generally play in distinct sections (e.g. sections of violinists). This means that in the orchestra scenario, different modes of communication coexist: a complementary coordination with the conductor and other musicians, in parallel with the synchronization with musicians of the same group.

In the present study, we aimed at understanding how these different modes are co-regulated during natural interaction and whether these dynamics are associated to different channels of communication. We had a full orchestra playing music while we recorded bow and head kinematics (instrumental and ancillary movements) of a first and second section of violinists (four violinists in each section) as well as the hand and head kinematics of two different conductors. In one experimental condition we applied a perturbation to the orchestra sensorimotor information flow. The perturbation consisted in half-turn rotation of the first section of violinists so that they faced the second section and couldn't see the conductor anymore. This perturbation modifies the perceptuo-motor context of

the first section of violinists, placing also the second section and the conductor into a novel playing situation. By doing so, we analyzed musicians to musicians and musicians to conductor inter-group coordination as well as intra-group synchronization (modes of communication), through different *channels* of communication (instrumental and ancillary movements) during different playing situations (normal and perturbed).

We hypothesized a co-regulation of the different modes of communication to adapt to the different situations. In the perturbed context, we expected a general increase of the influence of the second section on other musicians and conductor, together with a decrease of the influence of the first section. In parallel, the second section may decrease intra-group synchronization strength to focus on communication with the first section and conductor. On the contrary, the first section may need to rely more on his own and increase intra-group synchronicity. Finally, the two channels of communication should exhibit different modulations across groups, *modes* and conditions. For instance, information channeled through arm movements, essential for playing, may be less affected by the perturbation than the ancillary channel.

(b)　　Materials and Methods

Subjects

A full orchestra consisting of 8 violinists (2 sections of four violinists: S1 and S2) and 10 instrumentalists participated in the study along with two professional conductors (C1 and C2). Data were collected from the two violinists' sections and conductors. Each violinists section counted four players. The study was approved by the SIEMPRE Project Management Committee and adhered to the standards laid down in the Declaration of Helsinki. All participants gave written informed consent before participating. The synchronized multimodal recordings of the musicians obtained for this experiment as well as the details of the SIEMPRE platform for multimodal recordings are made available to the research community from the EU ICT FET SIEMPRE web pages (http://www.siempre.infomus.org).

Procedure

The two conductors and the orchestra executed two pieces of music selected from their repertoire so that their performance could already be at plateau and thus showing no learning during the experiment. The music pieces were excerpts from the ouverture of "Signor Bruschino" by Rossini and the Vivaldiana, terzo movimento by Malipiero (lasting around five minutes each). Two experimental conditions were tested (Figure 19A), which only differ by the way one section (henceforth, first section, S1) interacts with the conductor and the other section (henceforth, second

section, S2). In one condition (normal condition, Norm; Figure 19 in blue), S1 violinists - lined in a single row - were able to see C, but not S2 violinists. This condition kept the standard position of the musicians. In the second condition (perturbed condition; Figure 19 in red) S1 violinists - still lined in a single row - were able to see S2 violinists, but not C (since they were facing backwards with respect to him). This condition altered the standard position of the musicians. The two pieces were repeated six times (three times with C1 and three other times with C2) in each experimental condition (normal versus perturbed). In total, 24 trials were recorded.
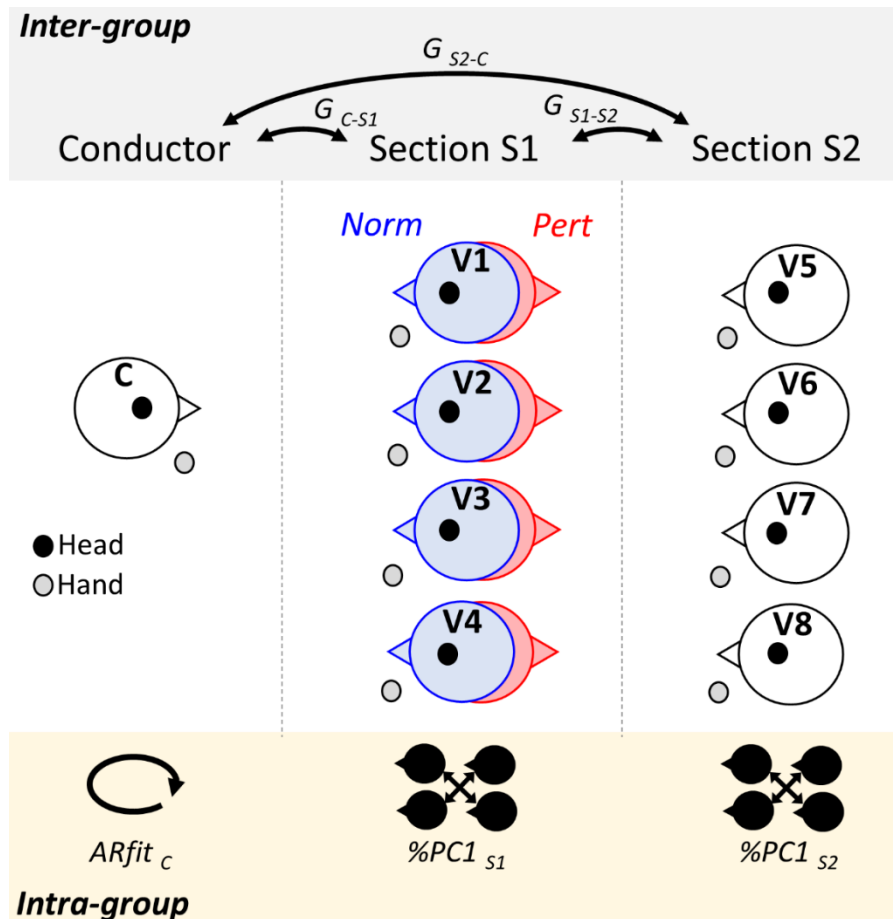
Figure 19: Orchestra musicians' position and associated computations.
The section in the middle represents the respective position of musicians in the orchestra: conductor (C), first section of violinists (S1; 4 violinists: V1, V2, V3 and V4) and second section of violinists (S2; 4 violinists: V5, V6, V7 and V8). In the normal condition (Norm; blue), S1 faces the conductor. In the perturbed condition (Pert; red), S1 rotates 180° facing S2. For each participant we recorded head (black dot) and hand (grey dot) kinematics. We extracted the pattern of communication at the group-level (between S1, S2 and C) using conditional Granger Causality (G) as shown in the top of the figure. Additionally, intra-group coordination, as described in the lower part of the figure, was computed via principal component analysis (%PC1) and an index of predictability of the conductor behavior (using the goodness of fit of the associated auto-regressive model; ARfit).

Apparatus and set-up

Movement data were collected (1000Hz) by using a Qualisys motion capture system equipped with 7 cameras, integrated with the EyesWeb XMI platform: http://www.infomus.org/eyesweb_ita.php (Volpe, Alborno, et al. 2016), including audio and physiological signals (not used here). Each violinist was equipped with passive markers of the Qualisys motion capture system. More specifically, for each player and conductor one marker was placed on the head and two markers were placed above the eyebrows. An additional marker was placed on the bows of the players and on the baton of the conductors. After data tracking by using the Qualisys Track Manager software, the data was exported and analyzed in MATLAB.

Data pre-processing and analysis

Data pre-processing and Granger causality analysis. We first used the spline method to handle the missing data in the 3D trajectories. The spline method interpolates missing data with continuous third order derivatives. We then computed the magnitude of the acceleration from each 3D trajectory (as done in (D'Ausilio et al. 2012)). Each musician time-series on each trial was normalized (to z-scores) and outliers values (>6std) were set as absent values (NaN) and interpolated when the gap was smaller than 200 frames (i.e. 2sec).

Inter-group communication: Granger causality analysis. Granger causality analysis was then carried out on the preprocessed acceleration waveforms. According to Granger formalism, a signal X Granger-causes (or G-causes) a signal Y if the past values of X contains information that helps predict Y above and beyond the information contained in the past values of Y alone. Thus, a Granger-causality score (gca) was defined between each pair of musicians as the log-likelihood ratio of the degree to which the prior time series of a musician X (causing variable) contributes to predict the current status of a musician Y (dependent variable), over and above the degree to which it is predicted by its own prior time series while conditional on the remaining musicians time-series (conditional variables). The use of conditional allow to take into account the influence of musicians out of the tested pair to avoid misinterpretation due to multiple sources of information (D'Ausilio et al. 2012; Chang et al. 2017). Gca was evaluated (pairwise), every 500 milliseconds on 3-s sliding windows using the "Granger Causality connectivity analysis" Matlab toolbox (Seth 2010). Windows containing more than one third (i.e. 166ms) of absent values were not used in the analysis (less than 5% of the total windows number). The Granger Causality computation is similar to the one used in (Badino et al. 2014; D'Ausilio et al. 2012). From this point, we will represent gca of X on Y by the notations $G_{X->Y}$ or X->Y.

We were interested in the causality relations between the conductor and each section of violinists (S1 and S2). This analysis is illustrated in Figure 19 (upper panel). We performed three different types of Conditional Granger causality computations: (1) Causality between each conductor and violinists of S1 (taken separately): defining as causing variable the conductor, as dependent variable each S1 violinist separately and the other way around [conditional variable: musicians in S2 - taken separately]. (2) Causality between each conductor and violinists of S2 (taken separately): defining as causing variable the conductor, as dependent variable each S2 violinist separately and the other way around [conditional variable: musicians in S1 - taken separately]. (3) Causality between the violinists of S1 and S2 (taken separately): defining as causing variable each S1 violinist separately, as dependent variable S2 violinists separately and the other way around [conditional variable: the conductor]. In these three analyses, we computed gca between each pair of musicians on each 3s window. When the causality between the two variables was significant, we kept the gca value otherwise this value was set to 0. Finally, gca values were averaged across conditional variables and musicians of same section, to get one value per group (i.e. C->S1, S1->C, C->S2, S2->C, S1->S2, S2->S1). Thus, for each experimental condition, the output matrix consisted of 6 columns (the number of causal relation) and thousands of lines (the number of considered windows).

Intra-section synchronization: Principal Component Analysis. To evaluate the level of synchronization between violinists' movements of each section of violinists (playing the same score), we used a principal component analysis (PCA (Jolliffe 2002)). PCA is a standard statistical technique generally used to extract a low-dimensional structure from a high-dimensional dataset. Dimensionality reduction method are classically used in the motor synergies field to extract invariant/similar features across time between muscle or kinematic parameters. In particular, PCA has been used to characterize the degree of covariance across time of different body segments in whole-body movements (e.g. locomotion (Hicheur, Terekhov, and Berthoz 2007); reaching (Berret et al. 2009)). Here, PCA was performed on the acceleration profiles of the four violinists of each section (Figure 19, lower panel), windowed and pre-processed in the same way as Granger Causality analysis. Mathematically, the method involves the eigenvalue decomposition of a dataset covariance matrix in order to find the principal directions in the high-dimensional space. For each of the windows, we considered an input matrix composed of 300 rows (temporal frames) and 4 columns (the acceleration profiles of the four violinists in each section) to which we applied the Matlab *princomp* function, after a zscore normalization of the input matrix. The PCA gives four principal components (PC) each written as a linear combination of the initial waveforms (the four violinists' acceleration profile). The variance accounted for (VAF) by the first principal component (noted PC1%) is defined as the ratio between the first eigenvalue and the sum of all the eigenvalues. The

VAF represents the degree to which the linear combination associated to each PC is able to approximate the initial dataset. A high PC1% value means that the trajectory in the space of angles is close to a straight line (i.e., all angles were linearly correlated together) while, a low PC1% value indicates that one principal component is not sufficient to describe precisely the trajectories.

Conductor behavior predictability: auto-regressive model's fitting. We evaluated the level of predictability of conductors' behavior (Figure 19, lower panel) as goodness of fit of the linear autoregressive model computed on the conductor acceleration profile extracted from hand and head data separately. We modelled the conductor acceleration profile via a linear autoregressive model in the same way we computed it for Granger Causality analysis and on the same sliding windows parameters. The optimal order of the model was determined via the Akaike's information criterion and the goodness-of-fit (ARfit) was measured as the sum of squares of the residuals, for each sliding window.

<u>Statistical analyses</u>

Inter-group and intra-group data did not follow a normal distribution according to normality tests (Kolmogorov–Smirnov) and the variances were also not homogeneous according to statistical tests (Levene). We, therefore, used a two-tail independent samples Welch's t-test (already used on same type of data in (Badino et al. 2014)). In the Welch's t-test the assumption of normality is not critical for large samples (Geary 1947) as it is the case for our data set. More importantly, Welch developed an approximation method for comparing the means of two independent populations when their variances are not necessarily equal (Welch 1947). Because Welch's modified t-test is not derived under the assumption of equal variances, it allows the comparison of two populations without first having to test for equality of variance.

Based on the data extracted in the "inter group interactions", we made three different set of comparisons, repeated twice (once for head data, once for wand data). (1) For the normal condition, we ran 5 comparisons: C->S1 vs S1->C, C->S2 vs S2->C, S1->S2 vs S2->S1, C->S1 vs C->S2, S1->C vs S2->C. The other possible comparisons were not performed because they were not informative for the study (e.g. C->S1 vs S2->C) or comparing elements of different nature (e.g. C->S1 vs S2->S1). (2) For the perturbed condition, we ran the same 5 comparisons as in (1). (3) Across the two experimental conditions, we ran 6 comparisons: C->$S1_{NORM}$ vs C->$S1_{PERT}$, C->$S2_{NORM}$ vs C->$S2_{PERT}$, $S1$->C_{NORM} vs $S1$->C_{PERT}, $S2$->C_{NORM} vs $S2$->C_{PERT}, $S1$->$S2_{NORM}$ vs $S1$->$S2_{PERT}$, $S2$->$S1_{NORM}$ vs $S2$->$S1_{PERT}$.

Based on the data extracted in "intra-section synchronization", we made four comparisons by kinematic parameters: $\%PC1_{S1\ NORM}$ vs $\%PC1_{S1\ PERT}$, $\%PC1_{S2\ NORM}$ vs $\%PC1_{S2\ PERT}$, $\%PC1_{S1\ NORM}$ vs $\%PC1_{S2\ NORM}$, $\%PC1_{S1\ PERT}$ vs $\%PC1_{S2\ PERT}$. Finally, based on the data extracted in "conductor

behavior predictability", we made two comparisons by kinematic parameters: ARfit $_{NORM}$ vs ARfit $_{PERT}$.

In all these analyses, the p-level was corrected for multiple comparisons with the Benjamini and Hochberg false discovery rate procedure. We reported in the results part the corrected p-value, and the value of the test statistic. We considered as marginally significant the statistical comparison for which the p-value before correction was inferior to 0.05. All analyses were conducted using the Matlab Statistics toolbox (Mathworks Inc.).

(c)   Results

Inter-group communication (Granger causality analysis)

Hand data. (1) In the normal condition, C G-caused S1 and S2 more than the other way around (Figure 20A, left panel; C<->S1: $p<0.001$, t=6.08; C<->S2: $p<0.001$, t=4.34). The gca of S1 on S2 was larger than the gca of S2 on S1 ($p<0.05$, t=2.63). No other significant differences appeared in Norm. (2) The pattern was the same in the perturbed condition (Figure 20A, right panel). C G-caused S1 and S2 more than the other way around (C<->S1: $p<0.001$, t=11.55; C<->S2: $p<0.001$, t=6.72). The gca of S1 on S2 was larger than the gca of S2 on S1 ($p<0.01$; t=3.31). In addition, the gca of S1 on the conductor was significantly smaller than the gca of S2 on the conductor ($p<0.01$, t=-3.17). No other significant differences appeared in Perturbed. (3) A significant decrease from Norm to Pert appeared in the gca of S1 on C ($p<0.05$, t=2.73). We found no additional significant change between the two conditions (Figure 20A, lower blue rectangle).

Head data. (1) In the normal condition, no significant difference appeared between the gca of C on S1 and S2 compared to the inverse relation (Figure 20B, left panel; C<->S1: p=0.29; C<->S2: p=0.40). A significant difference was found between the gca of S1 on S2 and S2 on S1: $G_{S1->S2}$ being higher than $G_{S2->S1}$ ($p<0.001$; t=3.72). In addition, the gca of C on S1 was larger than C on S2 ($p<0.001$; t=3.69). No other significant difference appeared in Norm. (2) In the perturbed condition (Figure 20B, right panel), C G-caused S1 significantly more than the inverse ($p<0.001$; t=5.64). In addition, the significant difference between the gca of S1 on S2 and S2 on S1 changed of direction compared to Norm: $G_{S1->S2}$ being smaller than $G_{S2->S1}$ ($p<0.01$; t=-2.69). Additionally, the gca of S2 on C was larger than the one of S1 on C ($p<0.001$; t=-7.89). No other significant differences appeared in Pert. (3) Comparing the two experimental conditions (Figure 20B, lower blue rectangle), we found a significant increase of $G_{C->S2}$ ($p<0.001$; t=-4.32) and $G_{S2->C}$ ($p<0.001$; t=-3.87) and a significant decrease of $G_{S1->C}$ ($p<0.001$; t=6.47) and $G_{S1->S2}$ ($p<0.001$; t=5.90) in Pert compared to Norm.
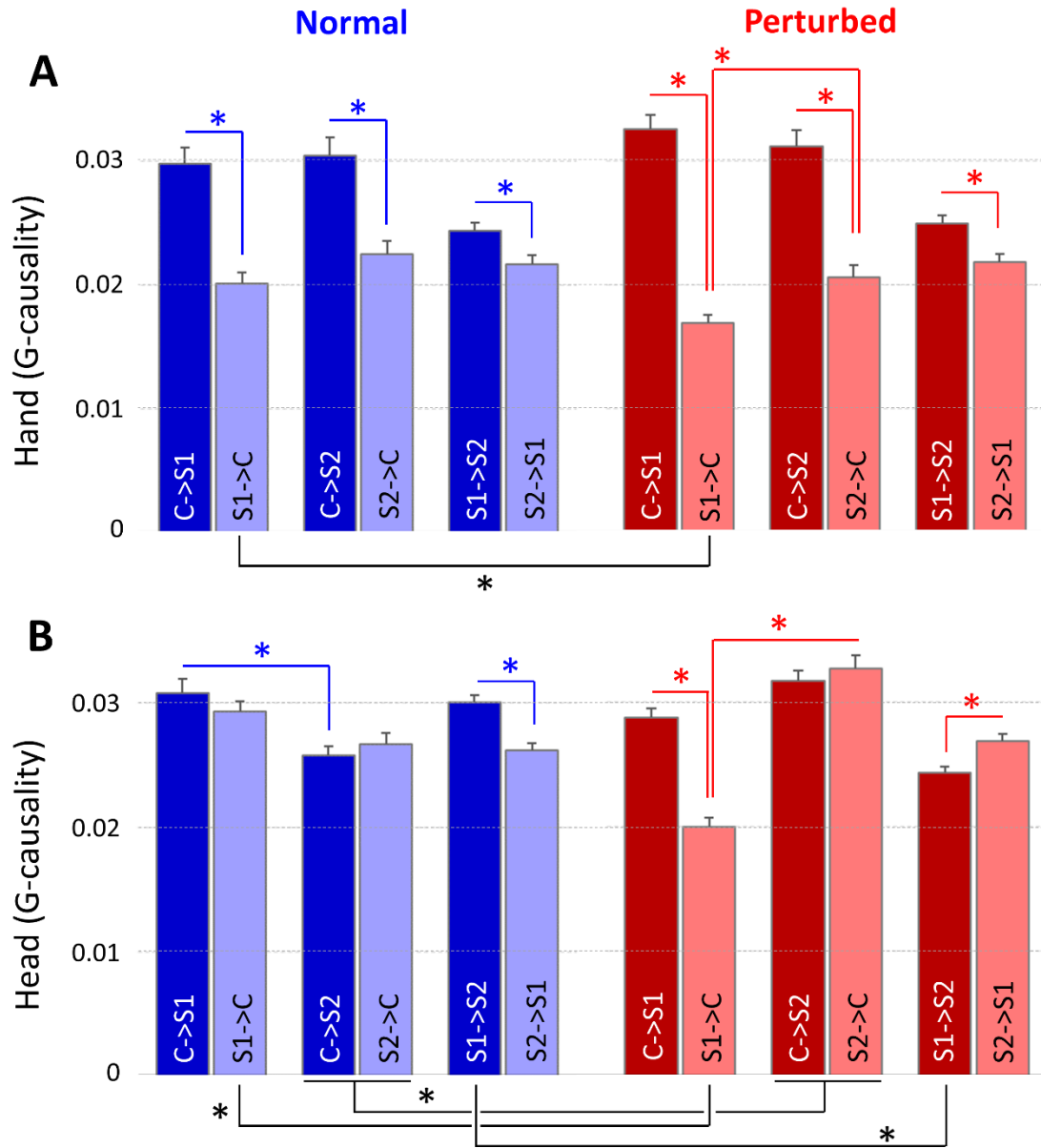
Figure 20: Inter-group coordination (gca).

Values extracted from Hand (A) and Head (B) acceleration profiles are shown for the normal (left side) and perturbed conditions (right side). Statistical differences within each condition are marked by colored lines on the top of each histogram. Statistical differences between conditions (Norm vs Pert) are represented by black lines under each histogram.

Intra-section synchronization (Principal component analysis)

Hand data. The %PC1 increased from Norm to Pert for S1 (Figure 21B, left panel; $p<0.01$; $t=-3.22$) while decreased for S2 ($p<0.001$; $t=4.03$). In addition, %PC1 was larger for S1 compared to S2 in the two experimental conditions (Norm: $p<0.001$; $t=7.11$; Pert: $p<0.001$; $t=12.97$).

Head data. A similar pattern of results was found for head data. The %PC1 increased from Norm to Pert for S1 (Figure 21B, right panel; $p<0.001$; $t=-5.35$) while decreased for S2 ($p<0.01$; $t=3.25$). In

102

addition, %PC1 was larger for S1 compared to S2 in the two experimental conditions (Norm: p<0.001; t=4.42; DoF=5450; Pert: p<0.001; t=12.03).
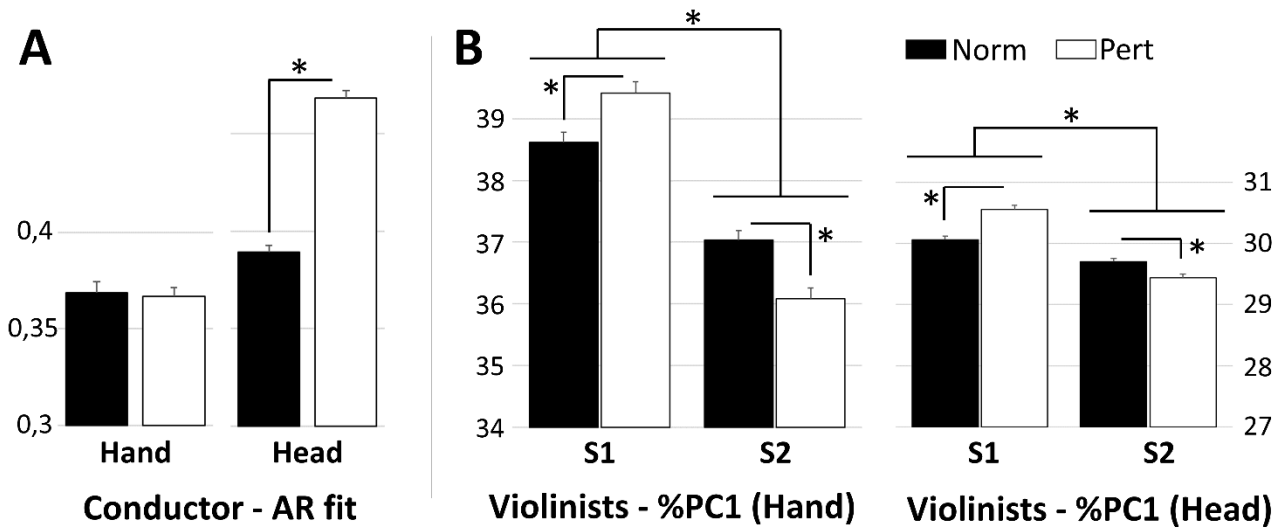
Figure 21: Intra-group synchronization (ARfjt and PCA).
(A) Predictability of the conductor behavior (ARfit). The autoregressive model was computed on the conductors, from hand and head data separately for the two experimental conditions normal (black) and perturbed (white). (B) Intra-section synchronization as indexed by the percentage of reconstruction of the first principal component (%PC1). PCA analysis was run on hand (middle panel) and head (right panel) acceleration profiles of the four violinists of each section (S1 and S2). Statistical differences are represented by black lines on the top of each histogram.

Conductor behavior predictability: auto-regressive model's fitting

Hand data. The goodness of fit of the autoregressive model for the hand data was not different in the two conditions Norm and Pert (p=0.81; t: 0.25; Figure 21A).

Head data. The goodness of fit of the autoregressive model for the head data was significantly smaller in Norm compared to Pert (p<0.001; t=-14.95; Figure 21A).

(d)   Discussion

Social interaction requires mastering the integration of multimodal sources of information to achieve efficient interpersonal coordination. Behavioral adaptation and synchronization are fundamentally based on predictive mechanisms and on the ability to use previous experience and context to guide perceptual processes while interaction unfolds (Donnarumma et al. 2017). Recently, an important resurgence of interest has emerged towards the exploration of human cognition in its true context, which is fundamentally interactive (Schilbach et al. 2013; Hari et al. 2015). Within this stream, ensemble musicians have been described as a powerful model to investigate complex non-verbal communication (D'Ausilio, Novembre, et al. 2015). The analysis of multi-agent kinematics via the

Granger Causality method has shown important promise (D'Ausilio et al. 2012). For instance, in orchestra, this method allowed the extraction of group-level information flow (D'Ausilio et al. 2012) which is associated to the quality of the musical output. Furthermore, by applying perturbations to the communication flow in quartets, subsequent studies showed rapid ensemble adaptation to sensorimotor information exchange (Badino et al. 2014; Chang et al. 2017). The present study tackled two fundamental scientific questions that had not been explored in previous experiments: whether different channels of communication exist and carry information differentially within the group (e.g. inter-group coordination and intra-group synchronization).

Regarding the different channels of communication, successful interaction generally requires that participants send and receive subtle messages in the form of various motor gestures. Musician's movements may generally be separated into instrumental and ancillary. In violinists, upper limbs movements are directly linked to the production of a music while head and trunk oscillation may carry additional information at the phrase level (Poggi 2011; Gritten and King 2011). For instance, subjective evaluation of conductors' faces movements were rated higher in expressivity, whereas arms movements were judged higher in amount of musical information (Wöllner 2008). Our results demonstrate that the pattern of sensorimotor information carried by two body parts (head and hand) are distinct (see Figures 22 for a schematic representation of main inter-group results). Hand kinematics exhibit a robust leader-follower relationship between the conductor and the two violinists' sections. This pattern is substantially not affected by the experimental manipulation of the sensorimotor information flow (perturbed condition) except for a decrease in communication between the first section and the conductor. The fact that the perturbation did not dramatically alter the information exchanged via instrumental movements suggests that an important role of memory, score reading and residual sensory cues. Indeed, musicians train for several hours and may rely on rehearsal memory to cope with the perturbation, at least for what concern pure instrumental execution. At the same time, there is also a clear directionality of the information flow from conductor to musicians, which confirms the idea of a predominant role of the conductor in the group management (Atik 1994). In head data, the perturbation produced clear alteration of the communication pattern. Communication between the first section and the conductor or the second section was reduced. At the same time, the bidirectional communication between the second section and the conductor increased, potentially as a compensatory strategy. In fact, the first section provided larger causal drive towards the second section, which, in the perturbed case, was transformed into a significant leadership of the second section over the first. During the perturbation, the first section no longer had visual contact with the conductor, significantly reducing his role in leading orchestra dynamics. At the same time, although violinists of the second section did not actually change their position, they are the only

ones establishing direct face-to-face communication with both first section and conductor. Correspondingly, our results suggest that S2 musicians were implicitly invested with far more centrality in orchestra coordination dynamics. In general, the distinct modulation of head versus hand kinematic parameters provides a demonstration of the multi-level complexity of musicians' coordination.
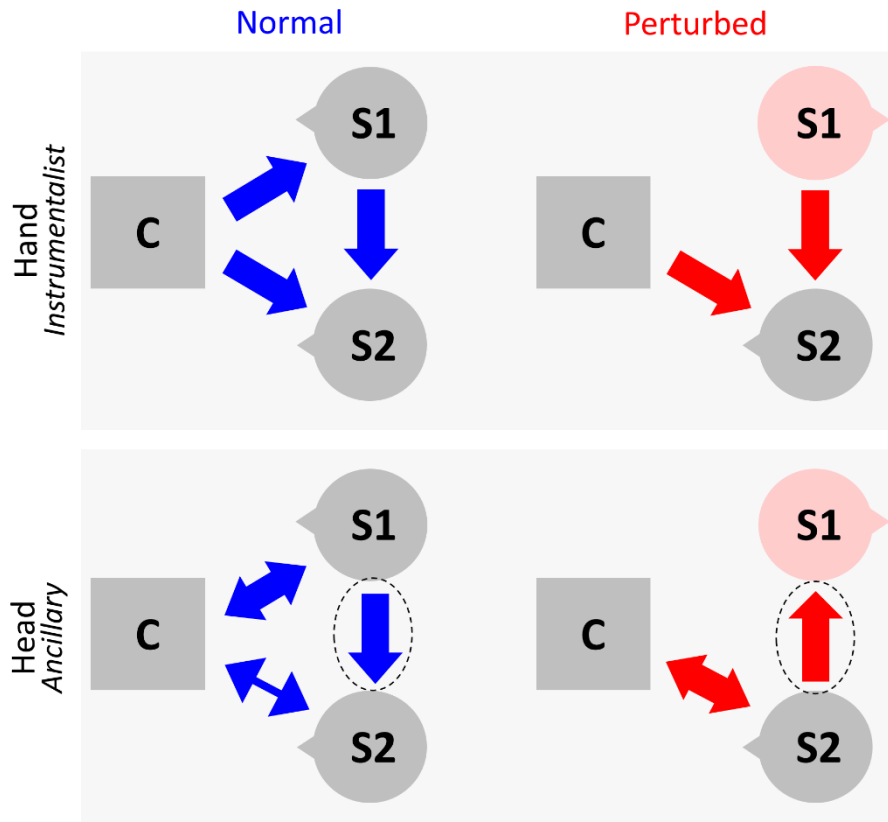
Figure 22: Schematic representation of inter-group coordination results.
Schematic representation of the main results for inter-group Granger-Causality analysis (i.e. inter-group coordination) across the conductor (C) and the two sections of violinists (S1 and S2). Results associated to the two channels, hand and head, are displayed respectively in the upper and lower panel. Directional arrows illustrate inter-group coordination (C, S1 and S2), in the normal (blue) and perturbed (red) condition. Arrows thickness represents the interaction's strength. A bidirectional arrow indicates similar gca values for the two directions (i.e. group 1 G-causes group 2, as much as group 2 G-causes group 1). On the opposite, a unidirectional arrow indicates the direction of the larger gca value (e.g. group 1 G-causes more group 2, than the inverse).

In the orchestra scenario an important aspect is played by the co-regulation of inter-group and intra-group communication (see Figures 23 for a schematic representation of main intra-group results). Indeed, each violinist must exchange information with other musicians of the same section (playing the same musical score) and with other participants (playing different parts). We used PCA to complement inter-group Gca analysis with an estimation of intra-section synchrony. Both kinematic parameters highlighted similar pattern of results. Due to the lack of communication with the

conductor, the first section became more synchronous, in the probable attempt to maximize performance accuracy. On the contrary, the second section that was endowed with the central role of being the communication hub, reduced intra-group coordination. This may be driven by a need to gain the necessary degrees of freedom to lead communication with S1 and be the sole interlocutor of the conductor. Therefore, here we show that to modulate inter-group dynamics, violinists had to penalize synchronization at the intra-group level.
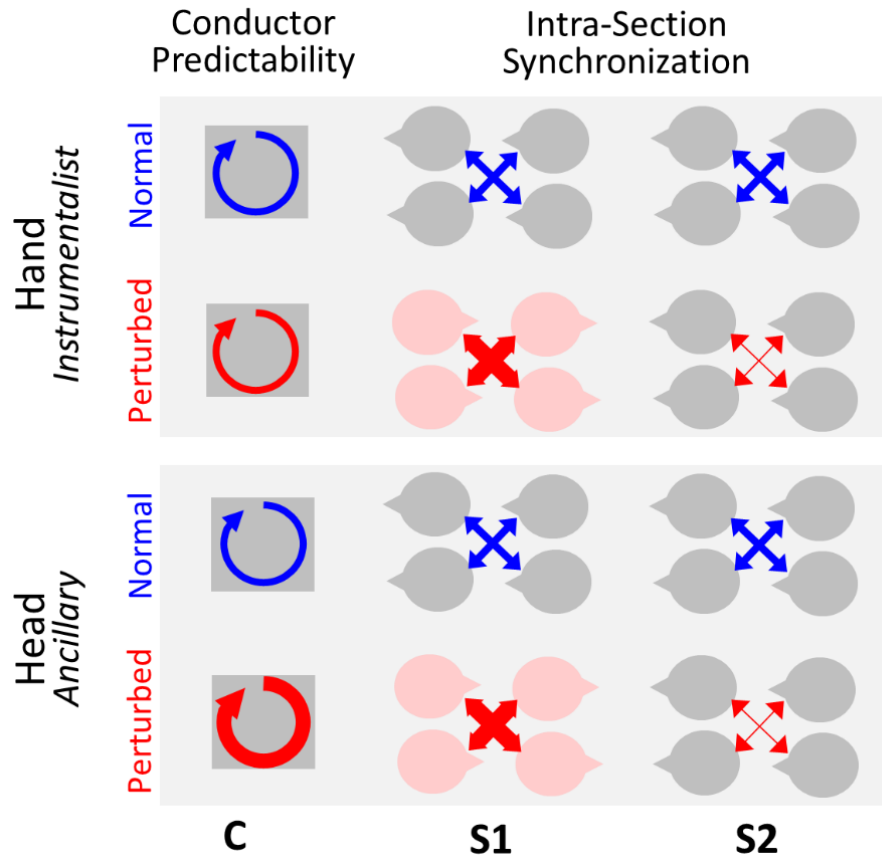

Figure 23: Schematic representation of intra-group synchronization results.
Schematic representation of the main results for intra-group analysis. Results associated to the two channels, hand and head, are displayed respectively in the upper and lower panel. Circular arrows displayed in the left panel represent the strength of conductor predictability (ARfit). Middle and right panels represent the intra-group synchronization's (%PC1) for both sections of violinists. Thickness of the arrow represent the strength of the effect in each experimental condition: normal (blue) and perturbed (red).

In general, any complex human interaction may require a mixture of action synchronization and imitation (Keller, Novembre, and Hove 2014) together with coordination in complementary actions (Sebanz, Bekkering, and Knoblich 2006). Although these two modes of interaction may naturally co-occur, it is difficult to explore them together in an experimentally controlled environment. Using the specificity of the orchestra scenario we explored here the interaction of intra-group dynamics

(dominated by synchronous behaviors) and inter-group dynamics (characterized by complementary action coordination).

Furthermore, we found an increase in conductor predictability following the perturbation, on head data only. Increasing behavioral predictability is a strategy already described for leaders in dyadic interaction (D'Ausilio, Badino, et al. 2015; Vesper et al. 2011). It may be an implicit coordination strategy helping the follower to build up a reliable internal model of the partners' behavior. Indeed, predictive models, built through practice and previous experiences, may guide individual action into an efficient coordination with peers (Wolpert, Doya, and Kawato 2003; Novembre et al. 2014; Sebanz and Knoblich 2009; Ramnani and Miall 2004). Behavioral predictions are confronted with sensorial feedbacks (Kilner and Frith 2007; Friston, Kilner, and Harrison 2006) and may help to coordinate actions requiring fast and precise temporal coordination (Knoblich, Butterfill, and Sebanz 2011), in which information can be sampled only intermittently. In professional musicians, extensive training may allow the construction of a detailed model of the piece and associated interactions. This model may, in turn, allow a good performance even in sub-optimal conditions, such as the one designed here. Indeed, extensive musical training has been associated with anatomo-functional changes (Münte, Altenmüller, and Jäncke 2002; Zatorre, Chen, and Penhune 2007) paralleled by enhanced ability to discriminate subtle changes in others' performance via predictive action simulation (D'Ausilio et al. 2010; Candidi et al. 2014).

In conclusion, our work highlights the multidimensionality of group coordination by evidencing different channels of communication (ancillary versus instrumental movements), affecting coordination at different levels (inter-group versus intra-group) tapping into different modes of cooperation (complementary versus synchronous). The co-regulation of these elements is the key musicians use to flexibly adapt to perturbation of the normal information flow and that is potentially shared with other non-musical complex ecological interaction.

General discussion

Perceiving another individual's movement recruits similar motor activations in the observer's brain. This empirical observation has substantiated the claim that engagement of the motor system may be essential in supporting other's action discrimination (Rizzolatti and Craighero 2004). At the same time, this process appears essential in supporting joint action, especially when imitative behaviors are critical. However, to simply imitate another person's action/s in many situations may not be an effective nor required response. Indeed, successful interaction often requires complementary rather than emulative behavior. In this PhD work, we first question a strict version of the direct matching hypothesis (simulative account) by using a series of single-subjects action observation protocols. In a second step, by means of multi-agent tasks, we investigated how visual cues affect various forms of complementary human-to-human interactions.

In the first study, we evaluated, side-by-side, motor evoked potential (MEPs) and TMS-evoked kinematics parameters (MEKs) to characterize action observation effects in humans. The experimental protocol consisted in a classical action observation task (Gangitano, Mottaghy, and Pascual-Leone 2001), involving reaching-grasping towards either one of two objects with different sizes (thus affording power or precision grip). We observed a critical modulation related to the grip type (precision vs. power grip): larger responses for precision grip. However, our results showed a clear difference between the two kinds of measures. While MEPs increased only for finger extensors and only in one session, a significant MEKs modulation was found for the thumb elevation angle in both recording sessions. These results demonstrate that the use of TMS-evoked thumb kinematics provides a greater reproducibility of AOEs and acts thus as a more effective measure than MEPs in describing the motor activities triggered by action observation.

We propose that this greater consistency of MEKs compared to MEPs directly arise from the principles of modularity and redundancy of the human motor system. Due to technical limitations (e.g. finding stimulation intensity and optimal site of stimulation), most action observation TMS studies focused on the recording of very few muscles. However, in general (in a realistic scenario), little discriminative information about the executed movement can be extracted from the activity of one (or few) muscle(s)). Indeed, the same amount of EMG activity in one muscle is present in many different actions and is not necessarily predictive of the action goal. In particular, neural control of arm and hand movements is the consequence of many adjustments at the muscular level (Bernstein 1967; Bizzi et al. 1984; Gribble 2003), following possibly a synergistic organization (D'Avella et al.

2006; Gentner and Classen 2006; Santello, Baud-Bovy, and Jörntell 2013; Leo et al. 2016). For example, finger extensors activation while lifting an object is in principle against the goal of applying forces onto an object, but it is necessary, via co-contraction with the flexors, to stabilize fingers and wrist joints. Therefore, recording from finger extensor only, would not allow to discriminate the act of opening or closing fingers. More importantly, similar kinematic patterns (and thus visual appearance) can be associated to different muscle recruitment over time and space. In this regard, redundancy and invariance principles in action execution (Guigon, Baraduc, and Desmurget 2007; Sporns and Edelman 1993; Flash and Hochner 2005), suggest that the functional kinematic output, more than the activities of (few) muscles, provides the best action goal description.

Furthermore, this same fact (motor redundancy) challenges the theoretical idea of a direct match between the observed and executed action (Kilner 2012; D'Ausilio, Bartoli, and Maffongelli 2015b; Hilt et al. 2017). Indeed, a strict version of the direct-matching hypothesis (Rizzolatti, Fogassi, and Gallese 2001; Rizzolatti and Craighero 2004; Rizzolatti and Sinigaglia 2016) can explain inferences when a direct relationship exists between muscle recruitment, movement kinematics and behavioral goals (e.g. simple finger movements). However, it is less clear how this proposal deals with the observation of complex movements (i.e. multi-joint movements) in which different joint configurations, as well as spatio-temporal patterns of muscle activity, can equally be used to reach the same behavioral goal (Bernstein 1967). At the execution level, the multiple degrees of freedom problem is solved by the use of a limited number of possible kinematic configurations of the biomechanical chain (e.g. "ankle" and "hip" strategies for postural control; Berret et al. 2009; Horak and Nashner 1986), although a handful of kinematic solutions are biomechanically valid. On the top of that, everyone carries his own robust and yet unique way of moving (Individual Motor Signature – IMS; Hilt et al. 2016; Słowiński et al. 2016).

We suggest, in our second study, that these two properties of human motor control lead to a new one-to-one mapping that is function of everyone own way of moving (individual motor strategy, IMS). To prove it, we combined an action execution and action observation task of a whole-body reaching action, naturally evoking different IMS. Our results demonstrated that in this type of multi-joint action, AOE cannot be summarized into a common standard pattern, but are instead subject-dependent. CSE was modulated at the single subject level according to the "distance" between actors' and observer's IMS: large CSE modulations are associated with the observation of a different IMS. In agreement with the predictive coding account, these results evidenced that the sensorimotor system computes differences rather than similarities, while observing complex but perfectly common whole-

body actions. In this model, prior motor knowledge provides critical top-down signals that are integrated with bottom-up sensory-based processing (Friston 2010b; Friston, Mattout, and Kilner 2011). To do so, a comparison between predicted and observed kinematic information generates a prediction error signal that is used to update the representation of other's action.

In a third study, we pursued this idea in investigating sensorimotor recruitment during action error observation. If a direct matching between observer and actor exists (Rizzolatti, Fogassi, and Gallese 2001; Rizzolatti and Craighero 2004; Rizzolatti and Sinigaglia 2016), observation of an error should activate the same inhibitory mechanisms at play during error execution (Buch et al. 2010). Differently, the predictive coding hypothesis suggests that an error should produce a greater surprise and thus a larger difference between expected and observed action-related information (Kilner, Friston, and Frith 2007; Urgen and Miller 2015; Sartori et al. 2015). Greater mismatch should then translate into a greater activity of the AON at the moment in which an error is detected. To investigate the fine temporal dynamic of excitation/inhibition balance during action error processing, we used different TMS protocols (single pulse, short intracortical inhibition - sICI, and intracortical facilitation - ICF) over M1, at three different time points following the action error (+120, +180 and +240 ms). We demonstrated an early (120 ms) reduction of inhibition for the observation of a motor execution error, while the control error elicited a similar effect but with a longer latency (240 ms). Effects were observed for sICI but not for ICF, suggesting that the neural mechanisms involved in detecting action execution errors mainly consist in the modulation of intracortical inhibitory circuits only. These results show that observing erroneous actions does not elicit increased inhibition as it would be predicted by the classic view about motor mirroring of other's action (direct matching). Instead, the release from inhibition could be explained by the greater mismatch with respect to the generated top-down predictions (predictive coding).

Altogether, the first set of studies highlight the incongruences associated to a pure simulative account of action observation in humans. Instead, the predictive coding hypothesis might better to bridge the gap between the fields of motor control and action observation.

However, everyday interactions are generally far more complex than a simple action observation. Thus, in a second part of this PhD, we investigated how sensory information and in particular vision are used by the interacting partners to efficiently coordinate with each other.

We first focused on the motor planning part and muscular anticipation during a dyadic non-verbal interaction. The interaction consisted of two individuals face to face. One individual (the carrier) holds a cylindric object in his left hand while the second individual (the partner) had to reach, grasp and lift this object with his right hand. Two conditions were added to manipulate visual information (the carrier had eyes closed or opened) and proprioceptive information (dyadic condition: the partner is another person, self condition: the partner is also the carrier) of the carrier. In such a context, the central nervous system anticipates movement consequences and produces anticipatory postural adjustments accordingly (APAs; Hugon, Massion, and Wiesendanger 1982; Massion et al. 1999). Our results showed that when participants performed the task themselves in full vision (Self, Eyes open), muscle activities of the carrier (wrist flexor and extensors) showed an early APAs (before the grasping onset). Without visual input (Self, Eyes closed), muscle activities changes on the load-bearing hand were significantly delayed (after the grasping onset), similarly to the classical APAs (Hugon, Massion, and Wiesendanger 1982; Dufossé, Hugon, and Massion 1985; Massion et al. 1999). Importantly, APAs were present in the joint action scenario, though significantly reduced by the lack of efference copy signal. Indeed, when the partner performed the unloading in full vision (Dyadic, Eyes open), the APA was present but significantly attenuated in amplitude, suggesting that motor predictions based on visual cues only requires the integration of the successive somatosensory feedback to fully deploy the appropriate postural response. This demonstrates that during haptic interaction, beside self-motor representations, individuals adapt the cooperation dynamics to the sensory signals coming from various sources.

As shown here dyadic setups allow to study the mechanisms underlying fast inter-individual coordination. However, such dyadic context represents a very narrow part of daily life human interactions. For instance, during a conversation, information is sampled through multiple channels (e.g. vision, audition), sometimes in parallel (e.g. information in the foreground and information from the background) and at different temporo-spatial scales (e.g. slow whole-body movements versus fast lip motions). At the same time, different kinds of information may be conveyed in parallel through different channels. Therefore, proper quantification of group coordination is today one of the key missing elements to understand how humans manage to interact with others by efficiently selecting, processing and sending information. In this context, ensemble musicians have been proposed as an ideal model, by keeping the key multidimensional properties of natural sensorimotor interaction but allowing good experimental control. Few previous studies have started to model sensorimotor information flows across musicians, by relying on kinematic recordings.

However, none of them were able to quantify the existence of multiple channels of communication as well as their respective role in efficient coordination. To fill this gap, the last study of this PhD examined movement-based interaction dynamics in an orchestra (one conductor and two sections of violinists), adapting to a perturbation affecting their normal pattern of sensorimotor communication. Using Granger Causality and Principal Component analyses, we revealed the existence of different channels of communication (hand Vs. head kinematics) associated to different modes of interaction (inter-group coordination versus intra-group synchronization). The instrumental movements (hand kinematics) were substantially not affected by the perturbation, suggesting an important role of memory and score reading. On the contrary, within ancillary movements (head kinematics), we could observe how the perturbation reshaped the social architecture of the orchestra. Indeed, the role of the second line of violinists evolved and, through a parallel regulation of inter-group coordination and intra-group synchronization, achieved status of mediator between the conductor and the first line.

Our results demonstrate that complex, multi-agent, non-verbal interaction is achieved via the co-regulation of different modes of cooperation (complementary versus synchronous) through different channels of communication (ancillary versus instrumental movements) to flexibly adapt to contextual constraints. Beyond the context of orchestra, multi-layer sensorimotor communication seems to be the key humans use to flexibly communicate between each other in interactive sensorimotor tasks.

In conclusion, this PhD aimed at introducing classical motor control techniques, tasks and ideas into the action observation field of research. The results we obtained, speak in favor of a predicting coding idea of how the motor system support others' action perception, as opposed to a strict version of the classical direct matching hypothesis. At the same time, the computation of an accurate prediction and an associated error signal seem to be essential to allow effective and fast-paced interaction. In this regard, our interactive studies both showed that action observation is relevant but is only a small part of the coordination process. A successful investigation of this complexity should go through the analysis of multiple spatial and temporal scales, as we only started with the last orchestra study.

I'd like to conclude by saying that I see classical passive action observation tasks extremely effective in evidencing the neural underpinnings of action discrimination. However, I'm aware that far greater complexity - and richness – awaits us behind the true context where action observation/execution deploy their true function. Here we just started to scratch the surface of this complexity by exporting the classical phenomena APA into a dyadic fast interaction scenario and by exploiting the known group coordination expertise demonstrated by ensemble musicians.

Additional works

In parallel of the works presented above, I took part during my PhD in different projects presented below.

1. The neural oscillatory markers of phonetic convergence during verbal interaction

Abstract: During a conversation, the neural processes supporting speech production and perception over-lap in time and, based on context, expectations and the dynamics of interaction, they are also continuously modulated in real time. Recently, the growing interest in the neural dynamics underlying interactive tasks, in particular in the language domain, has mainly tackled the temporal aspects of turn-taking in dialogs. Besides temporal coordination, an under-investigated phenomenon is the implicit convergence of the speakers toward a shared phonetic space. Here, we used dual electroencephalography (dual-EEG) to record brain signals from subjects involved in a relatively constrained interactive task where they were asked to take turns in chaining words according to a phonetic rhyming rule. We quantified participants' initial phonetic finger prints and tracked their phonetic convergence during the interaction via a robust and automatic speaker verification technique. Results show that phonetic convergence is associated to left frontal alpha/low-beta desynchronization during speech preparation and by high-beta suppression before and during listening to speech in right centro-parietal and left frontal sectors, respectively. By this work, we provide evidence that mutual adaptation of speech phonetic tar-gets, correlates with specific alpha and beta oscillatory dynamics. Alpha and beta oscillatory dynamics may index the coordination of the "when" as well as the "how" speech interaction takes place, reinforcing the suggestion that perception and production processes are highly interdependent and co-constructed during a conversation.

My contribution: data recording and paper writing

2. Motor cortical inhibition during concurrent action execution and observation

Abstract: Action Execution (AE) and Action Observation (AO) are intertwined in interaction and coordination. They are most often engaged at the same time to coordinate different plans of actions and recruit a common set of motor areas. The neurophysiological mechanisms allowing interindividual coordination during concurrent action execution and observation are however substantially unknown. To assess the effect of observed actions (i.e. performed by others') on observer's motor performance, we asked participants to perform hand opening and closing movements while observing the same or a different action (either hand opening and closure). By Transcranial Magnetic Stimulation we found that Cortical Silent Periods (CSP, measuring GABAB-mediated cortical inhibitory strength), but not Corticospinal Excitability (CSE, measuring the effects of various inputs on the corticospinal neurons), showed a significant interaction between AE and AO. These results suggest that GABAB-mediated motor cortical inhibition may be an important component to adapt one's motor execution to the contextual cues provided by other's actions.

My contribution: data recording and analysis and paper writing

This work is currently submitted in Neuroimage:

P Cardellicchio, E Dolfini, PM Hilt, L Fadiga and A D'Ausilio. Motor cortical inhibition during concurrent action execution and observation

3. **Attentional bias on motor control: is motor inhibition influenced by attentional reorienting?**

Abstract: Motor inhibition and attentional processing are tightly linked. Recent neurophysiological studies have shown that both processes might rely on similar cognitive and neural mechanisms (Wessel and Aron 2017). However, it remains unclear whether attentional reorientation influences inhibition of a subsequent action. Therefore, we combined two tasks that are commonly used in the motor inhibition and visual attention reorientation field [respectively: the stop-signal task (Logan and Cowan 1984) and the Posner endogenous cueing paradigm (Posner 1980)] to investigate how different aspects of visual attention modulate subsequent voluntary inhibition. Our results showed an increase in stopping-reaction time after a reorientation of attention only. This suggests a specific impairment of inhibitory control when a reorientation of visual attention is needed. These findings support the idea of a selective influence of attention reorientation on subsequent motor inhibition (stop signal). This may be linked to the "circuit breaker" hypothesis, proposing that attention reorientation toward an unexpected event "resets" the ongoing processes to allow the analysis of the potentially behaviorally relevant visual events (Corbetta, Patel, and Shulman 2008).

My Contribution: data analysis, results interpretation and manuscript writing

4. Space-by-time modular decomposition effectively describes whole-body muscle activity during upright reaching in various directions

Abstract: The modular control hypothesis suggests that motor commands are built from precoded modules whose specific combined recruitment can allow the performance of virtually any motor task. Despite considerable experimental support, this hypothesis remains tentative as classical findings of reduced dimensionality in muscle activity may also result from other constraints (biomechanical couplings, data averaging or low dimensionality of motor tasks). Here we assessed the effectiveness of modularity in describing muscle activity in a comprehensive experiment comprising 72 distinct point-to-point whole-body movements during which the activity of 30 muscles was recorded. To identify invariant modules of a temporal and spatial nature, we used a space-by-time decomposition of muscle activity that has been shown to encompass classical modularity models. To examine the decompositions, we focused not only on the amount of variance they explained but also on whether the task performed on each trial could be decoded from the single-trial activations of modules. For the sake of comparison, we confronted these scores to the scores obtained from alternative non-modular descriptions of the muscle data. We found that the space-by-time decomposition was effective in terms of data approximation and task discrimination at comparable reduction of dimensionality. These findings show that few spatial and temporal modules give a compact yet approximate representation of muscle patterns carrying nearly all task-relevant information for a variety of whole-body reaching movements.

My Contribution: protocol definition, data recording and analysis, results interpretation and manuscript writing

5. Deciphering the functional role of spatial and temporal muscle synergies in whole-body movements

Abstract: Voluntary movement is hypothesized to rely on a limited number of muscle synergies, the recruitment of which translates task goals into effective muscle activity. In this study, we investigated how to analytically characterize the functional role of different types of muscle synergies in task performance. To this end, we recorded a comprehensive dataset of muscle activity during a variety of whole-body pointing movements. We decomposed the electromyographic (EMG) signals using a space-by-time modularity model which encompasses the main types of synergies. We then used a task decoding and information theoretic analysis to probe the role of each synergy by mapping it to specific task features. We found that the temporal and spatial aspects of the movements were encoded by different temporal and spatial muscle synergies, respectively, consistent with the intuition that there should a correspondence between major attributes of movement and major features of synergies. This approach led to the development of a novel computational method for comparing muscle synergies from different participants according to their functional role. This functional similarity analysis yielded a small set of temporal and spatial synergies that describes the main features of whole-body reaching movements.

My Contribution: protocol definition, data recording and manuscript writing

6. Shifts in Key Time Points and Strategies for a Multisegment Motor Task in Healthy Aging Subjects

Abstract: In this study, we compared key temporal points in the whole body pointing movement of healthy aging and young subjects. During this movement, subject leans forward from a standing position to reach a target. As it involves forward inclination of the trunk, the movement creates a risk for falling. We examined two strategic time points during the task—first, the crossover point where the velocity of the center of mass (CoM) in the vertical dimension outstripped the velocity in the anteroposterior dimension and secondly, the time to peak of the CoM velocity profile. Transitions to stabilizing postures occur at these time points. They both occurred earlier in aging subjects. The crossover point also showed adjustments with target distance in aging subjects, while this was not observed in younger subjects. The shifts in these key time points could not be attributed to differences in movement duration between the two groups. Investigation with an optimal control model showed that the temporal adjustment as a function of target distance in the healthy aging subjects fits into a strategy that emphasized equilibrium maintenance rather than absolute work as a control strategy.

My Contribution: data analysis, results interpretation, manuscript writing

List of publications

Peer-reviewed Journals (*equal contributions)

Authié CN, <u>Hilt PM</u>, N'Guyen S, Berthoz A and Bennequin D (2015, Frontiers in Human Neuroscience), Differences in gaze anticipation for locomotion with and without vision. DOI: 10.3389/fnhum.2015.00312.

<u>Hilt PM</u>, Berret B, Papaxanthis C, Stapley P & Pozzo T (2016, Scientific Reports), Evidence for subjective values guiding posture and movement coordination in a free-endpoint whole-body reaching task. DOI: 10.1038/srep23868.

<u>Hilt PM</u>, Bartoli E, Ferrari E, Jacono M, Fadiga L & D'Ausilio A (2017, Cortex) Action observation effects reflect the modular organization of the human motor system. DOI: 10.1016/j.cortex.2017.07.020.

Cardellicchio P*, <u>Hilt PM</u>*, Olivier E, Fadiga L & D'Ausilio A (2018, Scientific Reports) Early modulation of short intra-cortical inhibition during action errors.

<u>Hilt PM</u> & Cardellicchio P (2018, Psychological Research) Attentional bias on motor control: is motor inhibition influenced by attentional reorienting?

<u>Hilt PM</u>, Delis I, Pozzo T & Berret B (2018, Frontiers in Comput. Neurosci.) Space-by-time modular decomposition effectively describes whole-body muscle activity during upright reaching in various directions.

Casteran M, <u>Hilt PM</u>, Mourey F, Manckoundia P, French R & Thomas E (2018, Journal of Gerontology) Shifts in Key Time Points and Strategies for a Multisegment Motor Task in Healthy Aging Subjects. doi:10.1093/gerona/gly066.

Delis I, <u>Hilt PM</u>, Pozzo T, Panzeri S & Berret B (2018, Scientific Reports) Deciphering the functional role of spatial and temporal muscle synergies in whole-body movements.

Mukerjee S, Badino L, <u>Hilt PM</u>, Tomassini A, Inuggi A, Fadiga L, Nguyen N & D'Ausilio A (2018,

Human Brain Mapping) The neural oscillatory markers of phonetic convergence during verbal interaction.

Conference papers

Authié CN, Hilt PM, N'Guyen S, Berthoz A and Bennequin D. Pourquoi le regard anticipe-t-il la trajectoire locomotrice ? Neurophysiologie Clinique / Clinical Neurophysiology (2012), 42(6):388-389. DOI: 10.1016/j.neucli.2012.09.012

Mukherjee S, Legou T, Lancia L, Hilt PM, Tomassini A, Fadiga L, D'Ausilio A, Badino L and Nguyen N. Analyzing vocal tract movements during speech accommodation. In: Interspeech 2018, Sep 2018, Hyderabad, India. ISCA, Proceedings of Interspeech 2018. DOI: 10.21437/Interspeech.2018-2084

Delis I, Hilt PM, Pozzo T and Berret B. Identification of spatial-temporal muscle synergies from EMG epochs of various durations: a time-warped tensor decomposition. In: Proceedings of the 4th International Conference on NeuroRehabilitation. ICNR 2018: 4th International Conference on NeuroRehabilitation, 16-20 Oct 2018, Pisa, Italy. Springer (In Press).

A D'Ausilio, P Cardellicchio, E Dolfini and PM Hilt. Motor processes in a multi-agent environment. 2018. International Journal of Psychophysiology 131:S49. DOI: 10.1016/j.ijpsycho.2018.07.148

References

Abreu, a M, E Macaluso, R T Azevedo, P Cesari, C Urgesi, and S M Aglioti. 2012. "Action Anticipation beyond the Action Observation Network: A Functional Magnetic Resonance Imaging Study in Expert Basketball Players." *The European Journal of Neuroscience* 35 (10): 1646–54. doi:10.1111/j.1460-9568.2012.08104.x.

Aglioti, Salvatore M., Paola Cesari, Michela Romani, and Cosimo Urgesi. 2008. "Action Anticipation and Motor Resonance in Elite Basketball Players." *Nature Neuroscience* 11 (9): 1109–16. doi:10.1038/nn.2182.

Ajemian, Robert, Alessandro D Ausilio, Helene Moorman, Emilio Bizzi, Robert Ajemian, Alessandro D Ausilio, Helene Moorman, et al. 2010. "Why Professional Athletes Need a Prolonged Period of Warm-Up and Other Peculiarities of Human Motor Learning Why Professional Athletes Need a Prolonged Period of Warm-Up and Other Peculiarities of Human Motor Learning" 2895 (March): 37–41. doi:10.1080/00222895.2010.528262.

Alaerts, Kaat, P. Senot, S. P. Swinnen, L. Craighero, N. Wenderoth, and L. Fadiga. 2010. "Force Requirements of Observed Object Lifting Are Encoded by the Observer's Motor System: A TMS Study." *European Journal of Neuroscience* 31 (6): 1144–53. doi:10.1111/j.1460-9568.2010.07124.x.

Alderisio, Francesco, Gianfranco Fiore, Robin N Salesse, Benoit G Bardy, and Mario di Bernardo. 2016. "Interaction Patterns and Individual Dynamics Shape the Way We Move in Synchrony." *ArXiv*. http://arxiv.org/abs/1607.02175.

Amoruso, Lucia, and Cosimo Urgesi. 2016. "Contextual Modulation of Motor Resonance during the Observation of Everyday Actions." *NeuroImage* 134. Elsevier Inc.: 74–84. doi:10.1016/j.neuroimage.2016.03.060.

Andersen, Richard A, and He Cui. 2009. "Review Intention , Action Planning , and Decision Making in Parietal-Frontal Circuits." *Neuron* 63 (5). Elsevier Ltd: 568–83. doi:10.1016/j.neuron.2009.08.028.

Arias, Pablo, Verónica Robles-García, Yoanna Corral-Bergantiños, Nelson Espinosa, Laura Mordillo-Mateos, Kenneth Grieve, Antonio Oliviero, and Javier Cudeiro. 2014. "Balancing the Excitability of M1 Circuitry during Movement Observation without Overt Replication." *Frontiers in Behavioral Neuroscience* 8: 316. doi:10.3389/fnbeh.2014.00316.

Aruin, Alexander S, and Mark L Latash. 1995. "Studied with Self-Induced and Externally Triggered Perturbations." *Experimental Brain Research* 106: 291–300.

Atik, Yaakov. 1994. "The Conductor and the Orchestra: Interactive Aspects of the Leadership

Process." *Leadership & Organization Development Journal* 15 (1): 22–28.

Avenanti, Alessio, Laura Annella, Matteo Candidi, Cosimo Urgesi, and Salvatore M. Aglioti. 2013. "Compensatory Plasticity in the Action Observation Network: Virtual Lesions of STS Enhance Anticipatory Simulation of Seen Actions." *Cerebral Cortex* 23 (3): 570–80. doi:10.1093/cercor/bhs040.

Avenanti, Alessio, Nadia Bolognini, Angelo Maravita, and Salvatore Maria Aglioti. 2007. "Somatic and Motor Components of Action Simulation." *Current Biology* 17 (24): 2129–35. doi:10.1016/j.cub.2007.11.045.

Avikainen, Sari, Nina Forss, and Riitta Hari. 2002. "Modulated Activation of the Human Si and Sii Cortices during Observation of Hand Actions." *NeuroImage* 15 (3): 640–46. doi:10.1006/nimg.2001.1029.

Aziz-Zadeh, Lisa, Fumiko Maeda, Eran Zaidel, John Mazziotta, and Marco Iacoboni. 2002. "Lateralization in Motor Facilitation during Action Observation: A TMS Study." *Experimental Brain Research* 144: 127–31. doi:10.1007/s00221-002-1037-5.

Badino, Leonardo, Alessandro D'Ausilio, Donald Glowinski, Antonio Camurri, and Luciano Fadiga. 2014. "Sensorimotor Communication in Professional Quartets." *Neuropsychologia* 55 (1). Elsevier: 98–104. doi:10.1016/j.neuropsychologia.2013.11.012.

Balconi, M., and C. Caldiroli. 2011. "Semantic Violation Effect on Object-Related Action Comprehension. N400-like Event-Related Potentials for Unusual and Incorrect Use." *Neuroscience* 197 (December): 191–99. doi:10.1016/j.neuroscience.2011.09.026.

Barchiesi, Guido, and Luigi Cattaneo. 2013. "Early and Late Motor Responses to Action Observation." *Social Cognitive and Affective Neuroscience* 8 (6): 711–19. doi:10.1093/scan/nss049.

Barlaam, Fanny, Médéric Descoins, Olivier Bertrand, Thierry Hasbroucq, Franck Vidal, Christine Assaiante, and Christina Schmitz. 2011. "Time-Frequency and ERP Analyses of EEG to Characterize Anticipatory Postural Adjustments in a Bimanual Load-Lifting Task." *Frontiers in Human Neuroscience* 5 (163): 1–9. doi:10.3389/fnhum.2011.00163.

Bartoli, Eleonora, Alessandro D'Ausilio, Jeffrey Berry, Leonardo Badino, Thomas Bever, and Luciano Fadiga. 2015. "Listener-Speaker Perceived Distance Predicts the Degree of Motor Contribution to Speech Perception." *Cerebral Cortex* 25 (2): 281–88. doi:10.1093/cercor/bht257.

Bartoli, Eleonora, Laura Maffongelli, Marco Jacono, and Alessandro D'Ausilio. 2014. "Representing Tools as Hand Movements: Early and Somatotopic Visuomotor Transformations." *Neuropsychologia* 61 (1). Elsevier: 335–44. doi:10.1016/j.neuropsychologia.2014.06.025.

Bates, A T, T P Patel, and P F Liddle. 2005. "External Behavior Monitoring Mirrors Internal Behavior Monitoring: Error-Related Negativity for Observed Errors." *Journal of Psychophysiology* 19: 281–88. doi:https://doi.org/10.1027/0269-8803.19.4.281.

Becchio, Cristina, Andrea Cavallo, Chiara Begliomini, Luisa Sartori, Giampietro Feltrin, and Umberto Castiello. 2012. "Social Grasping: From Mirroring to Mentalizing." *NeuroImage* 61 (1): 240–48. doi:10.1016/j.neuroimage.2012.03.013.

Becchio, Cristina, Luisa Sartori, Maria Bulgheroni, and Umberto Castiello. 2008. "The Case of Dr. Jekyll and Mr. Hyde: A Kinematic Study on Social Intention." *Consciousness and Cognition* 17 (3): 557–64. doi:10.1016/j.concog.2007.03.003.

Bekkering, Harold, Ellen R A De Bruijn, Raymond H. Cuijpers, Roger Newman-Norlund, Hein T. Van Schie, and Ruud Meulenbroek. 2009. "Joint Action: Neurocognitive Mechanisms Supporting Human Interaction." *Topics in Cognitive Science* 1 (2): 340–52. doi:10.1111/j.1756-8765.2009.01023.x.

Bennequin, Daniel, Ronit Fuchs, Alain Berthoz, and Tamar Flash. 2009. "Movement Timing and Invariance Arise from Several Geometries." *PLoS Computational Biology* 5 (7): e1000426. doi:10.1371/journal.pcbi.1000426.

Bernstein, N. A. 1967. *The Coordination and Regulation of Movements*. Pergamon P. Oxford.

Berret, Bastien, François Bonnetblanc, Charalambos Papaxanthis, and Thierry Pozzo. 2009. "Modular Control of Pointing beyond Arm ' s Length." *The Journal of Neuroscience* 29 (1): 191–205. doi:10.1523/JNEUROSCI.3426-08.2009.

Berret, Bastien, Enrico Chiovetto, Francesco Nori, and Thierry Pozzo. 2011. "Evidence for Composite Cost Functions in Arm Movement Planning : An Inverse Optimal Control Approach." *PLoS Computational Biology* 7 (10): 2–18. doi:10.1371/journal.pcbi.1002183.

Betti, Sonia, Umberto Castiello, and Luisa Sartori. 2015. "Kick with the Finger: Symbolic Actions Shape Motor Cortex Excitability." *European Journal of Neuroscience* 42 (10): 2860–66. doi:10.1111/ejn.13067.

Bisio, Ambra, Alessandra Sciutti, Francesco Nori, G Metta, Luciano Fadiga, Giulio Sandini, and Thierry Pozzo. 2014. "Motor Contagion during Human-Human and Human- Robot Interaction." *PloS One* 9 (8). doi:10.1371/journal.pone.0106172.

Bisio, Ambra, Natale Stucchi, Marco Jacono, Luciano Fadiga, and Thierry Pozzo. 2010. "Automatic versus Voluntary Motor Imitation: Effect of Visual Context and Stimulus Velocity." *PLoS ONE* 5 (10): 1–8. doi:10.1371/journal.pone.0013506.

Bizzi, E., N. Accornero, W. Chapple, and Neville Hogan. 1984. "Posture Control and Trajectory Formation during Arm Movement." *The Journal of Neuroscience* 4 (11): 2738–44.

Blair, Clifford R, and Walt Karniski. 1993. "An Alternative Method for Significance Testing of Waveform Difference Potentials." *Psychophysiology* 30: 518–24.

Blake, Randolph, and Maggie Shiffrar. 2007. "Perception of Human Motion." *Annual Review of Psychology* 58 (1). Annual Reviews: 47–73. doi:10.1146/annurev.psych.57.102904.190152.

Blakemore, Sarah Jayne, and Chris Frith. 2005. "The Role of Motor Contagion in the Prediction of Action." *Neuropsychologia* 43 (2 SPEC. ISS.): 260–67. doi:10.1016/j.neuropsychologia.2004.11.012.

Bond, Charles F., Adnan Omar, Urvashi Pitre, Brian R. Lashley, Lynn M. Skaggs, and C. T. Kirk. 1992. "Fishy-Looking Liars: Deception Judgment From Expectancy Violation." *Journal of Personality and Social Psychology* 63 (6): 969–77. doi:10.1037/0022-3514.63.6.969.

Borgomaneri, Sara, Francesca Vitale, and Alessio Avenanti. 2015. "Early Changes in Corticospinal Excitability When Seeing Fearful Body Expressions." *Scientific Reports* 5. Nature Publishing Group: 1–9. doi:10.1038/srep14122.

———. 2017. "Behavioral Inhibition System Sensitivity Enhances Motor Cortex Suppression When Watching Fearful Body Expressions." *Brain Structure and Function* 222 (7). Springer Berlin Heidelberg: 3267–82. doi:10.1007/s00429-017-1403-5.

Borgomaneri, Sara, Francesca Vitale, Valeria Gazzola, and Alessio Avenanti. 2015. "Seeing Fearful Body Language Rapidly Freezes the Observer's Motor Cortex." *Cortex* 65. Elsevier Ltd: 232–45. doi:10.1016/j.cortex.2015.01.014.

Borroni, Paola, and Fausto Baldissera. 2008. "Activation of Motor Pathways during Observation and Execution of Hand Movements." *Social Neuroscience* 3 (3–4): 276–88. doi:10.1080/17470910701515269.

Borroni, Paola, Marcella Montagna, Gabriella Cerri, and Fausto Baldissera. 2005. "Cyclic Time Course of Motor Excitability Modulation during the Observation of a Cyclic Hand Movement." *Brain Research* 1065 (1–2): 115–24. doi:10.1016/j.brainres.2005.10.034.

Botvinick, Matthew, Todd Braver, Deanna Barch, Cameron Carter, and Jonathan Cohen. 2001. "Conflict Monitoring and Cognitive Control." *Psychol Rev* 108 (3): 624–52. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=paovfte&NEWS=N&AN=00006832-200107000-00006.

Brass, Marcel, Ruth M. Schmitt, Stephanie Spengler, and Gy??rgy Gergely. 2007. "Investigating Action Understanding: Inferential Processes versus Action Simulation." *Current Biology* 17 (24): 2117–21. doi:10.1016/j.cub.2007.11.057.

Buccino, Giovanni, Stefan Vogt, Afra Ritzl, Gereon R. Fink, Karl Zilles, Hans Joachim Freund, and Giacomo Rizzolatti. 2004. "Neural Circuits Underlying Imitation Learning of Hand Actions: An

Event-Related FMRI Study." *Neuron* 42 (2): 323–34. doi:10.1016/S0896-6273(04)00181-3.

Buccolieri, Alessandro, Giovanni Abbruzzese, and John C Rothwell. 2004. "Relaxation from a Voluntary Contraction Is Preceded by Increased Excitability of Motor Cortical Inhibitory Circuits." *The Journal of Physiology* 558 (Pt 2). Wiley-Blackwell: 685–95. doi:10.1113/jphysiol.2004.064774.

Buch, Ethan R, Rogier B Mars, Erie D Boorman, and Matthew F S Rushworth. 2010. "A Network Centered on Ventral Premotor Cortex Exerts Both Facilitatory and Inhibitory Control over Primary Motor Cortex during Action Reprogramming." *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience* 30 (4): 1395–1401. doi:10.1523/JNEUROSCI.4882-09.2010.

Byrne, M D. 1993. "A Better Tool for the Cognitive Scientist's Toolbox: Randomization Statistics." *Proceedings of the Fifteenth Annual Conference of the Cognitive Science Society*.

Caetano, G., V. Jousmaki, and R. Hari. 2007. "Actor's and Observer's Primary Motor Cortices Stabilize Similarly after Seen or Heard Motor Actions." *Proceedings of the National Academy of Sciences* 104 (21): 9058–62. doi:10.1073/pnas.0702453104.

Calvo-Merino, Beatriz, Daniel E Glaser, Julie Grèzes, Richard E Passingham, and Patrick Haggard. 2005. "Action Observation and Acquired Motor Skills: An FMRI Study with Expert Dancers." *Cerebral Cortex* 15 (8): 1243–49. doi:10.1093/cercor/bhi007.

Calvo-Merino, Beatriz, Julie Grèzes, Daniel E Glaser, Richard E Passingham, and Patrick Haggard. 2006. "Seeing or Doing? Influence of Visual and Motor Familiarity in Action Observation." *Current Biology* 16 (19): 1905–10. doi:10.1016/j.cub.2006.07.065.

Candidi, Matteo, Lucia Maria Sacheli, Ilaria Mega, and Salvatore Maria Aglioti. 2014. "Somatotopic Mapping of Piano Fingering Errors in Sensorimotor Experts: TMS Studies in Pianists and Visually Trained Musically Naïves." *Cerebral Cortex* 24 (February): 435–43. doi:10.1093/cercor/bhs325.

Cardellicchio, Pasquale, Pauline M. Hilt, Etienne Olivier, Luciano Fadiga, and Alessandro D'Ausilio. 2018. "Early Modulation of Intra-Cortical Inhibition during the Observation of Action Mistakes." *Scientific Reports* 8 (1): 1784. doi:10.1038/s41598-018-20245-z.

Carpenter, Mark G., Allan L. Adkin, Lawrence R. Brawley, and James S. Frank. 2006. "Postural, Physiological and Psychological Reactions to Challenging Balance: Does Age Make a Difference?" *Age and Ageing* 35: 298–303. doi:10.1093/ageing/afl002.

Casile, Antonino, Eran Dayan, Vittorio Caggiano, Talma Hendler, Tamar Flash, and Martin A. Giese. 2010. "Neuronal Encoding of Human Kinematic Invariants during Action Observation." *Cerebral Cortex* 20 (7): 1647–55. doi:10.1093/cercor/bhp229.

Catmur, Caroline, Helge Gillmeister, Geoffrey Bird, Roman Liepelt, Marcel Brass, and Cecilia Heyes. 2008. "Through the Looking Glass: Counter-Mirror Activation Following Incompatible Sensorimotor Learning." *European Journal of Neuroscience* 28 (6): 1208–15. doi:10.1111/j.1460-9568.2008.06419.x.

Catmur, Caroline, Vincent Walsh, and Cecilia Heyes. 2007. "Sensorimotor Learning Configures the Human Mirror System." *Current Biology* 17 (17): 1527–31. doi:10.1016/j.cub.2007.08.006.

Cattaneo, Luigi, and Guido Barchiesi. 2011. "Transcranial Magnetic Mapping of the Short-Latency Modulations of Corticospinal Activity from the Ipsilateral Hemisphere during Rest." *Frontiers in Neural Circuits* 5 (October): 1–13. doi:10.3389/fncir.2011.00014.

Cattaneo, Luigi, F. Caruana, A. Jezzini, and Giacomo Rizzolatti. 2009. "Representation of Goal and Movements without Overt Motor Behavior in the Human Motor Cortex: A Transcranial Magnetic Stimulation Study." *The Journal of Neuroscience* 29 (36): 11134–38. doi:10.1523/JNEUROSCI.2605-09.2009.

Cattaneo, Luigi, F. Maule, Guido Barchiesi, and Giacomo Rizzolatti. 2013. "The Motor System Resonates to the Distal Goal of Observed Actions: Testing the Inverse Pliers Paradigm in an Ecological Setting." *Experimental Brain Research* 231 (1): 37–49. doi:10.1007/s00221-013-3664-4.

Cavallo, Andrea, Cristina Becchio, Luisa Sartori, Giulia Bucchioni, and Umberto Castiello. 2012. "Grasping with Tools: Corticospinal Excitability Reflects Observed Hand Movements." *Cerebral Cortex* 22 (3): 710–16. doi:10.1093/cercor/bhr157.

Cavallo, Andrea, Giulia Bucchioni, Umberto Castiello, and Cristina Becchio. 2013. "Goal or Movement? Action Representation within the Primary Motor Cortex." *European Journal of Neuroscience* 38 (10): 3507–12. doi:10.1111/ejn.12343.

Cavallo, Andrea, Cecilia Heyes, Cristina Becchio, Geoffrey Bird, and Caroline Catmur. 2014. "Timecourse of Mirror and Counter-Mirror Effects Measured with Transcranial Magnetic Stimulation." *Social Cognitive and Affective Neuroscience* 9 (8): 1082–88. doi:10.1093/scan/nst085.

Celnik, Pablo, Katja Stefan, Friedhelm Hummel, Julie Duque, Joseph Classen, and Leonardo G. Cohen. 2006. "Encoding a Motor Memory in the Older Adult by Action Observation." *NeuroImage* 29 (2): 677–84. doi:10.1016/j.neuroimage.2005.07.039.

Chang, Andrew, Steven R. Livingstone, Dan J. Bosnyak, and Laurel J. Trainor. 2017. "Body Sway Reflects Leadership in Joint Music Performance." *Proceedings of the National Academy of Sciences* 114 (21): E4134–41. doi:10.1073/pnas.1617657114.

Chen, R, J Classen, C Gerloff, P Celnik, E M Wassermann, M Hallett, and L G Cohen. 1997.

"Depression of Motor Cortex Excitability by Low-frequency Transcranial Magnetic Stimulation." *Neurology* 48 (5).

Clark, Shannon, François Tremblay, and Diane Ste-Marie. 2004. "Differential Modulation of Corticospinal Excitability during Observation, Mental Imagery and Imitation of Hand Actions." *Neuropsychologia* 42 (1): 105–12. doi:10.1016/S0028-3932(03)00144-1.

Classen, J, J Liepert, S P Wise, M Hallett, and L G Cohen. 1998. "Rapid Plasticity of Human Cortical Movement Representation Induced by Practice." *Journal of Neurophysiology* 79 (2): 1117–23. doi:citeulike-article-id:2143137.

Codrons, Erwan, Nicolò F. Bernardi, Matteo Vandoni, and Luciano Bernardi. 2014. "Spontaneous Group Synchronization of Movements and Respiratory Rhythms." *PLoS ONE* 9 (9). doi:10.1371/journal.pone.0107538.

Cole, K J, and James H Abbs. 1988. "Grip Force Adjustments Evoked by Load Force Perturbations of a Grasped Object." *Journal of Neurophysiology* 60 (4): 1513–22. doi:10.1152/jn.1988.60.4.1513.

Cook, Richard, Geoffrey Bird, Caroline Catmur, Clare Press, and Cecilia Heyes. 2014. "Mirror Neurons: From Origin to Function." *The Behavioral and Brain Sciences* 37 (2): 177–92. doi:10.1017/S0140525X13000903.

Corbetta, Maurizio, Gaurav Patel, and Gordon L. Shulman. 2008. "The Reorienting System of the Human Brain: From Environment to Theory of Mind." *Neuron* 58 (3): 306–24. doi:10.1016/j.neuron.2008.04.017.

Costantini, Marcello, Ettore Ambrosini, Pasquale Cardellicchio, and Corrado Sinigaglia. 2014. "How Your Hand Drives My Eyes." *Social Cognitive and Affective Neuroscience* 9 (5): 705–11. doi:10.1093/scan/nst037.

Costantini, Marcello, Gaspare Galati, Antonio Ferretti, Massimo Caulo, Armando Tartaro, Gian Luca Romani, and Salvatore Maria Aglioti. 2005. "Neural Systems Underlying Observation of Humanly Impossible Movements: An FMRI Study." *Cerebral Cortex* 15 (11): 1761–67. doi:10.1093/cercor/bhi053.

Coste, A, P Slowinski, K Tsaneva-Atanasova, B G Bardy, and L Marin. 2017. "Mapping Individual Postural Signatures." In *Studies in Perception & Action XIV*, edited by J A Weast-Knapp and G J Pepping. Taylor & Francis.

Cotugno, G, K Althoefer, and T Nanayakkara. 2016. "The Role of the Thumb: Study of Finger Motion in Grasping and Reachability Space in Human and Robotic Hands." In *IEEE Transactions on Systems, Man, and Cybernetics*.

Coxon, James P, Cathy M Stinear, and Winston D Byblow. 2006. "Intracortical Inhibition During

Volitional Inhibition of Prepared Action." *Journal of Neurophysiology* 95 (6): 3371–83. doi:10.1152/jn.01334.2005.

Cretu, Andreea Loredana, Kathy Ruddy, Maria Germann, and Nicole Wenderoth. 2018. "Motor Resonance in Primary Motor Cortex Reflects the Integration of Kinematic and Contextual Information in Accordance to a Bayesian Predictive Coding Framework." *BioRxiv*, 1–35. doi:http://dx.doi.org/10.1101/293977.

D'Ausilio, Alessandro, E Altenmüller, Olivetti M Belardinelli, and M Lotze. 2006. "Cross-Modal Plasticity of the Motor Cortex While Listening to a Rehearsed Musical Piece." *European Journal of Neuroscience* 24 (3): 955–58. doi:10.1111/j.1460-9568.2006.04960.x.

D'Ausilio, Alessandro, Leonardo Badino, Pietro Cipresso, Alice Chirico, Elisabetta Ferrari, Giuseppe Riva, and Andrea Gaggioli. 2015. "Automatic Imitation of the Arm Kinematic Profile in Interacting Partners." *Cognitive Processing* 16 (April 2016). Springer Berlin Heidelberg: 197–201. doi:10.1007/s10339-015-0699-4.

D'Ausilio, Alessandro, Leonardo Badino, Yi Li, Sera Tokay, Laila Craighero, Rosario Canto, Yiannis Aloimonos, and Luciano Fadiga. 2012. "Leadership in Orchestra Emerges from the Causal Relationships of Movement Kinematics." *PLoS ONE* 7 (5). doi:10.1371/journal.pone.0035757.

D'Ausilio, Alessandro, Eleonora Bartoli, and Laura Maffongelli. 2015a. "Grasping Synergies: A Motor-Control Approach to the Mirror Neuron Mechanism." *Physics of Life Reviews* 12 (February 2016). Elsevier B.V.: 91–103. doi:10.1016/j.plrev.2014.11.002.

———. 2015b. "Motor Control May Support Mirror Neuron Research with New Hypotheses and Methods. Reply to Comments on 'Grasping Synergies: A Motor-Control Approach to the Mirror Neuron Mechanism'." *Physics of Life Reviews* 12 (April 2016): 133–37. doi:10.1016/j.plrev.2015.02.005.

D'Ausilio, Alessandro, R Brunetti, F Delogu, C Santonico, and Olivetti M Belardinelli. 2010. "How and When Auditory Action Effects Impair Motor Performance." *Experimental Brain Research* 201 (2): 323–30. doi:10.1007/s00221-009-2044-6.

D'Ausilio, Alessandro, Laura Maffongelli, Eleonora Bartoli, M Campanella, Elisabetta Ferrari, Jeffrey Berry, and Luciano Fadiga. 2014. "Listening to Speech Recruits Specific Tongue Motor Synergies as Revealed by Transcranial Magnetic Stimulation and Tissue-Doppler Ultrasound Imaging." *Philosophical Transactions of the Royal Society B: Biological Sciences* 369 (1644): 20130418–20130418. doi:10.1098/rstb.2013.0418.

D'Ausilio, Alessandro, Giacomo Novembre, Luciano Fadiga, and Peter E Keller. 2015. "What Can Music Tell Us about Social Interaction ?" *Trends in Cognitive Sciences* 19 (3). Elsevier Ltd: 1–4. doi:10.1016/j.tics.2015.01.005.

D'Avella, Andrea, Alessandro Portone, Laure Fernandez, and Francesco Lacquaniti. 2006. "Control of Fast-Reaching Movements by Muscle Synergy Combinations." *The Journal of Neuroscience* 26 (30): 7791–7810. doi:10.1523/JNEUROSCI.0830-06.2006.

Daffertshofer, Andreas, Claudine J C Lamoth, Onno G. Meijer, and Peter J. Beek. 2004. "PCA in Studying Coordination and Variability: A Tutorial." *Clinical Biomechanics* 19 (4): 415–28. doi:10.1016/j.clinbiomech.2004.01.005.

Dayan, E., A. Casile, N. Levit-Binnun, M. A. Giese, T. Hendler, and T. Flash. 2007. "Neural Representations of Kinematic Laws of Motion: Evidence for Action-Perception Coupling." *Proceedings of the National Academy of Sciences* 104 (51): 20582–87. doi:10.1073/pnas.0710033104.

De Bruijn, Ellen R A, Ricarda I Schubotz, and Markus Ullsperger. 2007. "An Event-Related Potential Study on the Observation of Erroneous Everyday Actions." *Cognitive Affective & Behavioral Neuroscience* 7 (4): 278–85.

Dehaene, Stanislas, Michael I Posner, and Don M Tucker. 1994. "LOCALIZATION OF A NEURAL SYSTEM FOR ERROR DETECTION AND COMPENSATION." *Psychological Science* 5 (5): 303–5. http://journals.sagepub.com/doi/pdf/10.1111/j.1467-9280.1994.tb00630.x.

Desmet, Charlotte, and Marcel Brass. 2015. "Observing Accidental and Intentional Unusual Actions Is Associated with Different Subregions of the Medial Frontal Cortex." *NeuroImage* 122. Elsevier Inc.: 195–202. doi:10.1016/j.neuroimage.2015.08.018.

Devanne, H, B A Lavoie, and C Capaday. 1997. "Input-Output Properties and Gain Changes in the Human Corticospinal Pathway." *Exp Brain Res* 114 (2): 329–38. doi:10.1007/PL00005641.

Di Lazzaro, V, A Oliviero, M Meglio, B Cioni, G Tamburrini, P Tonali, and J C Rothwell. 2000. "Direct Demonstration of the Effect of Lorazepam on the Excitability of the Human Motor Cortex." *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology* 111 (5): 794–99. doi:10.1111/j.1439-0485.1994.tb00049.x.

di Pellegrino, Giuseppe, Luciano Fadiga, Leonardo Fogassi, Vittorio Gallese, and Giacomo Rizzolatti. 1992. "Understanding Motor Events: A Neurophysiological Study." *Experimental Brain Research* 91: 176–80.

Diedrichsen, Jörn, Timothy Verstynen, Andrew Hon, Steven L. Lehman, and Richard B. Ivry. 2003. "Anticipatory Adjustments in the Unloading Task: Is an Efference Copy Necessary for Learning?" *Experimental Brain Research* 148 (2): 272–76. doi:10.1007/s00221-002-1318-z.

Dikker, Suzanne, Lu Wan, Ido Davidesco, Lisa Kaggen, Matthias Oostrik, James McClintock, Jess Rowland, et al. 2017. "Brain-to-Brain Synchrony Tracks Real-World Dynamic Group Interactions in the Classroom." *Current Biology* 27 (9). Elsevier Ltd.: 1375–80.

doi:10.1016/j.cub.2017.04.002.

Donchin, O., S. Cardoso de Oliveira, and E. Vaadia. 1999. "Who Tells One Hand What the Other Is Doing: The Neurophysiology of Bimanual Movements." *Neuron* 23 (1): 15–18. doi:10.1016/S0896-6273(00)80748-5.

Donnarumma, Francesco, Marcello Costantini, Ettore Ambrosini, Karl J Friston, and Giovanni Pezzulo. 2017. "Action Perception as Hypothesis Testing." *Cortex* 89. Elsevier Ltd: 45–60. doi:10.1016/j.cortex.2017.01.016.

Donnarumma, Francesco, Haris Dindo, and Giovanni Pezzulo. 2017. "Sensorimotor Coarticulation in the Execution and Recognition of Intentional Actions." *Frontiers in Psychology* 8 (237). doi:10.3389/fpsyg.2017.00237.

Dufossé, M., M. Hugon, and J. Massion. 1985. "Postural Forearm Changes Induced by Predictable in Time or Voluntary Triggered Unloading in Man." *Experimental Brain Research* 60 (2): 330–34. doi:10.1007/BF00235928.

Dumas, Guillaume, Julien Laroche, and Alexandre Lehmann. 2014. "Your Body, My Body, Our Coupling Moves Our Bodies." *Frontiers in Human Neuroscience* 8 (December): 1–5. doi:10.3389/fnhum.2014.01004.

Dushanova, J, and J Donoghue. 2010. "Neurons in Primary Motor Cortex Engaged During Action Observation." *European Journal of Neuroscience* 31 (2): 386–98. doi:10.1111/j.1460-9568.2009.07067.x.Neurons.

Eklund, Anders, Thomas E. Nichols, and Hans Knutsson. 2016. "Cluster Failure: Why FMRI Inferences for Spatial Extent Have Inflated False-Positive Rates." *Proceedings of the National Academy of Sciences* 113 (33): 201602413. doi:10.1073/pnas.1602413113.

Elswijk, Gijs Van, Femke Maij, Jan-mathijs Schoffelen, Sebastiaan Overeem, Dick F Stegeman, and Pascal Fries. 2010. "Corticospinal Beta-Band Synchronization Entails Rhythmic Gain Modulation" 30 (12): 4481–88. doi:10.1523/JNEUROSCI.2794-09.2010.

Esposti, Roberto, Carlo Bruttini, Francesco Bolzoni, and Paolo Cavallari. 2017. "Anticipatory Postural Adjustments Associated with Reaching Movements Are Programmed According to the Availability of Visual Information." *Experimental Brain Research* 235 (5). Springer Berlin Heidelberg: 1349–60. doi:10.1007/s00221-017-4898-3.

Fadiga, Luciano, Laila Craighero, and Etienne Olivier. 2005. "Human Motor Cortex Excitability during the Perception of Others' Action." *Current Opinion in Neurobiology* 15 (2): 213–18. doi:10.1016/j.conb.2005.03.013.

Fadiga, Luciano, Leonardo Fogassi, G. Pavesi, and Giacomo Rizzolatti. 1995. "Motor Facilitation during Action Observation: A Magnetic Stimulation Study." *Journal of Neurophysiology* 73 (6):

2608–11.

Falck-Ytter, Terje, Gustaf Gredebäck, and Claes Von Hofsten. 2006. "Infants Predict Other People's Action Goals." *Nature Neuroscience* 9 (7): 878–79. doi:10.1038/nn1729.

Fessler, Daniel M.T., and Colin Holbrook. 2016. "Synchronized Behavior Increases Assessments of the Formidability and Cohesion of Coalitions." *Evolution and Human Behavior* 37 (6). Elsevier Inc.: 502–9. doi:10.1016/j.evolhumbehav.2016.05.003.

Fetz, E. E., and P. D. Cheney. 1980. "Postspike Facilitation of Forelimb Muscle Activity by Primate Corticomotoneuronal Cells." *Journal of Neurophysiology* 44 (4): 751–72.

Fetz, E. E., S. I. Perlmutter, Y. Prut, K. Seki, and S. Votaw. 2002. "Roles of Primate Spinal Interneurons in Preparation and Execution of Voluntary Hand Movement." *Brain Research Reviews* 40 (1–3): 53–65. doi:10.1016/S0165-0173(02)00188-1.

Finisguerra, Alessandra, Laura Maffongelli, Michela Bassolino, Marco Jacono, Thierry Pozzo, and Alessandro D'Ausilio. 2015. "Generalization of Motor Resonance during the Observation of Hand, Mouth, and Eye Movements." *Journal of Neurophysiology* 114 (4): 2295–2304. doi:10.1152/jn.00433.2015.

Flanagan, J Randall, and Roland S Johansson. 2003. "Action Plans Used in Action Observation." *Letters to Nature* 424 (Aug): 769–71. doi:10.1038/nature01861.

Flash, Tamar, and Binyamin Hochner. 2005. "Motor Primitives in Vertebrates and Invertebrates." *Current Opinion in Neurobiology* 15 (6): 660–66. doi:10.1016/j.conb.2005.10.011.

Flash, Tamar, and Neville Hogans. 1985. "The Coordination of Arm Movements: An Experimentally Confirmed Mathematical Model." *Journal of Neuroscience* 5 (7): 1688–1703.

Fluet, M.-C., Markus a Baumann, and Hansjörg Scherberger. 2010. "Context-Specific Grasp Movement Representation in Macaque Ventral Premotor Cortex." *Journal of Neuroscience* 30 (45): 15175–84. doi:10.1523/JNEUROSCI.3343-10.2010.

Franca, Michele, Luca Turella, Rosario Canto, Nicola Brunelli, Luisa Allione, Nico Golfré Andreasi, Marianna Desantis, Daniele Marzoli, and Luciano Fadiga. 2012. "Corticospinal Facilitation during Observation of Graspable Objects: A Transcranial Magnetic Stimulation Study." *PLoS ONE* 7 (11). doi:10.1371/journal.pone.0049025.

Frank, Mark G., and Paul Ekman. 1997. "The Ability to Detect Deceit Generalizes across Different Types of High-Stake Lies." *Journal of Personality and Social Psychology* 72 (6): 1429–39. doi:10.1037/0022-3514.72.6.1429.

Friston, Karl J. 2005. "A Theory of Cortical Responses." *Philosophical Transactions of the Royal Society B: Biological Sciences* 360 (1456): 815–36. doi:10.1098/rstb.2005.1622.

———. 2010a. "Is the Free-Energy Principle Neurocentric?" *Nature Reviews Neuroscience*, no. July.

Nature Publishing Group: 2–4. doi:10.1038/nrn2787-c2.

———. 2010b. "The Free-Energy Principle: A Unified Brain Theory?" *Nature Reviews Neuroscience* 11 (2). Nature Publishing Group: 127–38. doi:10.1038/nrn2787.

Friston, Karl J, L Harrison, and W Penny. 2003. "Dynamic Causal Modelling." *NeuroImage* 19 (4): 1273–1302. http://www.ncbi.nlm.nih.gov/pubmed/12948688.

Friston, Karl J, James M Kilner, and Lee Harrison. 2006. "A Free Energy Principle for the Brain." *Journal of Physiology* 100: 70–87. doi:10.1016/j.jphysparis.2006.10.001.

Friston, Karl J, Jérémie Mattout, and James M Kilner. 2011. "Action Understanding and Active Inference." *Biological Cybernetics* 104 (1–2): 137–60. doi:10.1007/s00422-011-0424-z.

Gangitano, Massimo, Felix M Mottaghy, and Alvaro Pascual-Leone. 2001. "Phase-Specific Modulation of Cortical Motor Output during Movement Observation." *Neuroreport* 12 (7): 1489–92. doi:10.1097/00001756-200105250-00038.

Geary, R C. 1947. "Testing for Normality." *Biometrika* 34 (3/4): 209–42.

Gehring, William J, Goss, Coles, Meyer, and Donchin. 1993. "A Neural System for Error Detection and Conpensation." *Psychological Science* 4 (6): 385–90. http://pss.sagepub.com/lookup/doi/10.1111/j.1467-9280.1993.tb00586.x%0Apapers3://publication/doi/10.1111/j.1467-9280.1993.tb00586.x.

Gentilucci, Maurizio, Ivan Toni, Elena Daprati, and Massimo Gangitano. 1997. "Tactile Input of the Hand and the Control of Reaching to Grasp Movements." *Experimental Brain Research* 114 (1): 130–37. doi:10.1007/PL00005612.

Gentner, Reinhard, and Joseph Classen. 2006. "Modular Organization of Finger Movements by the Human Central Nervous System." *Neuron* 52 (4): 731–42. doi:10.1016/j.neuron.2006.09.038.

Gentner, Reinhard, Susanne Gorges, David Weise, Kristin aufm Kampe, Mathias Buttmann, and Joseph Classen. 2010. "Encoding of Motor Skill in the Corticomuscular System of Musicians." *Current Biology* 20 (20). Elsevier Ltd: 1869–74. doi:10.1016/j.cub.2010.09.045.

Giese, Martin A., and Giacomo Rizzolatti. 2015. "Neural and Computational Mechanisms of Action Processing: Interaction between Visual and Motor Representations." *Neuron* 88 (1). Elsevier Inc.: 167–80. doi:10.1016/j.neuron.2015.09.040.

Grasso, R, L Bianchi, and F Lacquaniti. 1998. "Motor Patterns for Human Gait: Backward versus Forward Locomotion." *Journal of Neurophysiology* 80 (4): 1868–85. doi:10.1007/s002210050274.

Gribble, P. L. 2003. "Role of Cocontraction in Arm Movement Accuracy." *Journal of Neurophysiology* 89 (5): 2396–2405. doi:10.1152/jn.01020.2002.

Gritten, Anthony, and Elaine King. 2011. *New Perspectives on Music and Gesture*.

Guigon, Emmanuel, Pierre Baraduc, and Michel Desmurget. 2007. "Computational Motor Control: Redundancy and Invariance." *Journal of Neurophysiology* 97 (1): 331–47. doi:10.1152/jn.00290.2006.

Hamada, Masashi, Nagako Murase, Alkomiet Hasan, Michelle Balaratnam, and John C. Rothwell. 2013. "The Role of Interneuron Networks in Driving Human Motor Cortical Plasticity." *Cerebral Cortex* 23 (7): 1593–1605. doi:10.1093/cercor/bhs147.

Hammond, Geoffrey, and Ann Maree Vallence. 2007. "Modulation of Long-Interval Intracortical Inhibition and the Silent Period by Voluntary Contraction." *Brain Research* 1158 (1): 63–70. doi:10.1016/j.brainres.2007.05.014.

Hannah, Ricci, Lorenzo Rocchi, and John C Rothwell. 2018. "Observing Without Acting : A Balance of Excitation and Suppression in the Human Corticospinal Pathway ?" 12 (May): 1–10. doi:10.3389/fnins.2018.00347.

Hari, Riitta, N. Forss, S. Avikainen, E. Kirveskari, S. Salenius, and Giacomo Rizzolatti. 1998. "Activation of Human Primary Motor Cortex during Action Observation: A Neuromagnetic Study." *Proceedings of the National Academy of Sciences of the United States of America* 95 (25): 15061–65. doi:10.1073/pnas.95.25.15061.

Hari, Riitta, Linda Henriksson, Sanna Malinen, and Lauri Parkkonen. 2015. "Centrality of Social Interaction in Human Brain Function." *Neuron* 88 (1). Elsevier Inc.: 181–93. doi:10.1016/j.neuron.2015.09.022.

Hicheur, Halim, Alexander V Terekhov, and Alain Berthoz. 2007. "Intersegmental Coordination During Human Locomotion : Does Planar Covariation of Elevation Angles Reflect Central Constraints ? Intersegmental Coordination During Human Locomotion : Does Planar Covariation of Elevation Angles Reflect Central Constraints ?" *Journal of Neurophysiology*, 1406–19. doi:10.1152/jn.00289.2006.

Hilt, Pauline M., Bastien Berret, Charalambos Papaxanthis, Paul Stapley, and Thierry Pozzo. 2016. "Evidence for Subjective Values Guiding Posture and Movement Coordination in a Free-Endpoint Whole-Body Reaching Task." *Scientific Reports* 6 (April). Nature Publishing Group: 23868. doi:10.1038/srep23868.

Hilt, Pauline M, Eleonora Bartoli, Elisabetta Ferrari, Marco Jacono, Luciano Fadiga, and Alessandro D'Ausilio. 2017. "Action Observation Effects Reflect the Modular Organization of the Human Motor System." *Cortex* 95. Elsevier Ltd: 104–18. doi:10.1016/j.cortex.2017.07.020.

Hodges, J R, J Spatt, and K Patterson. 1999. "'What' and 'How': Evidence for the Dissociation of Object Knowledge and Mechanical Problem-Solving Skills in the Human Brain." *Proceedings of the National Academy of Sciences of the United States of America* 96 (16): 9444–48.

doi:10.1073/pnas.96.16.9444.

Horak, F B, and L M Nashner. 1986. "Central Programming of Postural Movements: Adaptation to Altered Support-Surface Configurations." *Journal of Neurophysiology* 55 (6): 1369–81. doi:3734861.

Hoshiyama, Minoru, Sachiko Koyama, Yoshihiro Kitamura, Motoko Shimojo, Shoko Watanabe, and Ryusuke Kakigi. 1996. "Effects of Judgement Process on Motor Evoked Potentials in Go/No-Go Hand Movement Task." *Neuroscience Research* 24 (4): 427–30. doi:10.1016/0168-0102(95)01013-0.

Huang, Ying Zu, Mark J. Edwards, Elisabeth Rounis, Kailash P. Bhatia, and John C. Rothwell. 2005. "Theta Burst Stimulation of the Human Motor Cortex." *Neuron* 45 (2): 201–6. doi:10.1016/j.neuron.2004.12.033.

Hudson, Matthew, Toby Nicholson, Rob Ellis, and Patric Bach. 2016. "I See What You Say: Prior Knowledge of Other's Goals Automatically Biases the Perception of Their Actions." *Cognition* 146. Elsevier B.V.: 245–50. doi:10.1016/j.cognition.2015.09.021.

Hugon, M., J. Massion, and M. Wiesendanger. 1982. "Anticipatory Postural Changes Induced by Active Unloading and Comparison with Passive Unloading in Man." *Pflugers Archiv European Journal of Physiology* 393 (4): 292–96. doi:10.1007/BF00581412.

Hunter, Micheal A, and Richard B May. 2003. "Statistical Testing and Null Distributions: What to Do When Samples Are Not Random." *Canadian Journal of Experimental Psychology* 57 (3): 176–88. doi:http://dx.doi.org/10.1037/h0087424.

Ilić, Tihomir V., Frank Meintzschel, Ulrich Cleff, Diane Ruge, Kirn R. Kessler, and Ulf Ziemann. 2002. "Short-Interval Paired-Pulse Inhibition and Facilitation of Human Motor Cortex: The Dimension of Stimulus Intensity." *The Journal of Physiology* 545 (1). Blackwell Publishing Ltd: 153–67. doi:10.1113/jphysiol.2002.030122.

Jankowska, E. 1992. "Interneuronal Relay in Spinal Pathways from Proprioceptors." *Progress in Neurobiology* 38: 335–78.

Jeannerod, M. 2001. "Neural Simulation of Action: A Unifying Mechanism for Motor Cognition." *NeuroImage* 14 (1 Pt 2): S103–9. doi:10.1006/nimg.2001.0832.

Johansson, Roland S., and J. Randall Flanagan. 2009. "Coding and Use of Tactile Signals from the Fingertips in Object Manipulation Tasks." *Nature Reviews Neuroscience* 10 (5): 345–59. doi:10.1038/nrn2621.

Jola, Corinne, Ali Abedian-Amiri, Annapoorna Kuppuswamy, Frank E. Pollick, and Marie Hélène Grosbras. 2012. "Motor Simulation without Motor Expertise: Enhanced Corticospinal Excitability in Visually Experienced Dance Spectators." *PLoS ONE* 7 (3).

doi:10.1371/journal.pone.0033343.

Jolliffe, I T. 2002. "Principal Component Analysis, Second Edition." *Encyclopedia of Statistics in Behavioral Science* 30 (3): 487. doi:10.2307/1270093.

Keil, Julian, Jana Timm, Iria Sanmiguel, Hannah Schulz, Jonas Obleser, and Marc Schönwiesner. 2014. "Cortical Brain States and Corticospinal Synchronization Influence TMS-Evoked Motor Potentials." *Journal of Neurophysiology* 111 (3): 513–19. doi:10.1152/jn.00387.2013.

Keller, Peter E, Giacomo Novembre, and Michael J Hove. 2014. "Rhythm in Joint Action: Psychological and Neurophysiological Mechanisms for Real-Time Interpersonal Coordination." *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 369 (1658): 20130394. doi:10.1098/rstb.2013.0394.

Kermadi, I, Y Liu, A Tempini, and E M Rouiller. 1997. "Effects of Reversible Inactivation of the Supplementary Motor Area (SMA) on Unimanual Grasp and Bimanual Pull and Grasp Performance in Monkeys." *Somatosensory & Motor Research* 14 (4): 268–80. doi:10.1080/08990229770980.

Killeen, Peter R. 2005. "Replicability, Confidence and Priors." *Amercican Psychological Society* 16 (12): 1009–12.

Kilner, James M. 2012. "More than One Pathway to Action Understanding." *Trends in Cognitive Sciences* 15 (8): 352–57. doi:10.1016/j.tics.2011.06.005.More.

Kilner, James M, Karl J Friston, and Chris D Frith. 2007. "The Mirror-Neuron System: A Bayesian Perspective." *NeuroReport* 18 (6): 619–23. doi:10.1097/WNR.0b013e3281139ed0.

Kilner, James M, and Chris D Frith. 2007. "Predictive Coding: An Account of the Mirror Neuron System." *Cognitive Processing* 8 (3): 159–66. doi:10.1007/s10339-007-0170-2.Predictive.

Kilner, James M, and Roger N Lemon. 2013. "What We Know Currently about Mirror Neurons." *Current Biology* 23 (23). Elsevier Ltd: R1057–62. doi:10.1016/j.cub.2013.10.051.

Kilner, James M, Claudia Vargas, Sylvie Duval, Sarah-Jayne Blakemore, and Angela Sirigu. 2004. "Motor Activation Prior to Observation of a Predicted Movement." *Nature Neuroscience* 7 (12). Nature Publishing Group: 1299–1301. doi:10.1038/nn1355.

Klein-Flügge, Miriam Cornelia, David Nobbs, Julia B Pitcher, and Sven Bestmann. 2013. "Variability of Human Corticospinal Excitability Tracks the State of Action Preparation." *The Journal of Neuroscience* 33 (13): 5564–72. doi:10.1523/JNEUROSCI.2448-12.2013.

Knoblich, Günther, Stephen Butterfill, and Natalie Sebanz. 2011. *Psychological Research on Joint Action. Theory and Data. Psychology of Learning and Motivation - Advances in Research and Theory*. Vol. 54. doi:10.1016/B978-0-12-385527-5.00003-6.

Kobayashi, Masahito, and Alvaro Pascual-Leone. 2003. "Transcranial Magnetic Stimulation in

Neurology." *Lancet Neurology* 2 (3): 145–56. doi:10.1016/S1474-4422(03)00321-1.

Koch, Giacomo, Viviana Versace, Sonia Bonnì, Federica Lupo, Emanuele Lo Gerfo, Massimiliano Oliveri, and Carlo Caltagirone. 2010. "Resonance of Cortico–cortical Connections of the Motor System with the Observation of Goal Directed Grasping Movements." *Neuropsychologia* 48 (12): 3513–20. doi:10.1016/j.neuropsychologia.2010.07.037.

Koelewijn, Thomas, Hein T. van Schie, Harold Bekkering, Robert Oostenveld, and Ole Jensen. 2008. "Motor-Cortical Beta Oscillations Are Modulated by Correctness of Observed Action." *NeuroImage* 40 (2): 767–75. doi:10.1016/j.neuroimage.2007.12.018.

Koul, Atesh, Andrea Cavallo, Caterina Ansuini, and Cristina Becchio. 2016. "Doing It Your Way: How Individual Movement Styles Affect Action Prediction." *PLoS ONE* 11 (10): 1–14. doi:10.1371/journal.pone.0165297.

Kraskov, a, R Philipp, S Waldert, G Vigneswaran, M M Quallo, R N Lemon, and Phil Trans R Soc B. 2014. "Corticospinal Mirror Neurons." *Philosophical Transactions of the Royal Society B* 369 (April): 20130174. doi:10.1098/rstb.2013.0174.

Kubicki, Alexandre, Lilian Fautrelle, Julien Bourrelier, Olivier Rouaud, and France Mourey. 2016. "The Early Indicators of Functional Decrease in Mild Cognitive Impairment." *Frontiers in Aging Neuroscience* 8 (AUG): 1–11. doi:10.3389/fnagi.2016.00193.

Kujirai, T, M D Caramia, J C Rothwell, B L Day, P D Thompson, A Ferbert, S Wroe, P Asselman, and C D Marsden. 1993. "CORTICOCORTICAL INHIBITION IN HUMAN MOTOR CORTEX." *Journal of Physiology* 471: 501–19.

Leo, Andrea, Giacomo Handjaras, Matteo Bianchi, Hamal Marino, Marco Gabiccini, Andrea Guidi, Enzo Pasquale Scilingo, et al. 2016. "A Synergy-Based Hand Control Is Encoded in Human Motor Cortical Areas." *ELife* 5 (FEBRUARY2016): 1–32. doi:10.7554/eLife.13420.

Leocani, L, L G Cohen, E M Wassermann, K Ikoma, and M Hallett. 2000. "Human Corticospinal Excitability Evaluated with Transcranial Magnetic Stimulation during Different Reaction Time Paradigms." *Brain : A Journal of Neurology*, June, 1161–73. http://www.ncbi.nlm.nih.gov/pubmed/10825355.

Leonard, Julia A, Ryan H Brown, and Paul J Stapley. 2009. "Reaching to Multiple Targets When Standing: The Spatial Organization of Feedforward Postural Adjustments." *Journal of Neurophysiology* 101 (4): 2120–33. doi:10.1152/jn.91135.2008.

Levin, Oron, Nicole Wenderoth, Maarten Steyvers, and Stephan P. Swinnen. 2003. "Directional Invariance during Loading-Related Modulations of Muscle Activity: Evidence for Motor Equivalence." *Experimental Brain Research* 148 (1): 62–76. doi:10.1007/s00221-002-1277-4.

Liepert, J, J Classen, L G Cohen, and M Hallett. 1998. "Task-Dependent Changes of Intracortical

Inhibition." *Experimental Brain Research* 118 (3): 421–26. http://www.ncbi.nlm.nih.gov/pubmed/9497149.

Logan, Gordon D., and W B Cowan. 1984. "On the Ability to Inhibit Thought and Action." *Psychol Rev* 91: 295–327.

Loporto, Michela, Paul S. Holmes, David J. Wright, and Craig J. McAllister. 2013. "Reflecting on Mirror Mechanisms: Motor Resonance Effects during Action Observation Only Present with Low-Intensity Transcranial Magnetic Stimulation." *PLoS ONE* 8 (5): e64911. doi:10.1371/journal.pone.0064911.

Ludbrook, John, and Hugh Dudley. 1998. "Why Permutation Tests Are Superior to t and F Tests in Biomedical Research." *The American Statistician* 52 (2): 127–32.

Macerollo, A., S. Bose, L. Ricciardi, M. J. Edwards, and James M Kilner. 2015. "Linking Differences in Action Perception with Differences in Action Execution." *Social Cognitive and Affective Neuroscience* 10 (8): 1121–27. doi:10.1093/scan/nsu161.

Maeda, Fumiko, Galit Kleiner-Fisman, and Alvaro Pascual-Leone. 2002. "Motor Facilitation While Observing Hand Actions: Specificity of the Effect and Role of Observer's Orientation." *Journal of Neurophysiology* 87 (3): 1329–35. doi:10.1152/jn.00773.2000.

Maffongelli, L., E. Bartoli, D. Sammler, S. Kölsch, C. Campus, E. Olivier, L. Fadiga, and A. D'Ausilio. 2015. "Distinct Brain Signatures of Content and Structure Violation during Action Observation." *Neuropsychologia* 75 (August 2015): 30–39. doi:10.1016/j.neuropsychologia.2015.05.020.

Manthey, Sophie, Ricarda I. Schubotz, and D. Yves Von Cramon. 2003. "Premotor Cortex in Observing Erroneous Action: An FMRI Study." *Cognitive Brain Research* 15 (3): 296–307. doi:10.1016/S0926-6410(02)00201-X.

Maris, Eric, and Robert Oostenveld. 2007. "Nonparametric Statistical Testing of EEG- and MEG-Data." *Journal of Neuroscience Methods* 164 (1): 177–90. doi:10.1016/j.jneumeth.2007.03.024.

Marzke, Mary W. 1997. "Precision Grips, Hand Morphology, and Tools." *American Journal of Physical Anthropology* 102 (1): 91–110. doi:10.1002/(SICI)1096-8644(199701)102:1<91::AID-AJPA8>3.0.CO;2-G.

Massion, Jean, Marat Ioffe, Christina Schmitz, François Viallet, and Radka Gantcheva. 1999. "Acquisition of Anticipatory Postural Adjustments in a Bimanual Load-Lifting Task: Normal and Pathological Aspects." *Experimental Brain Research* 128 (1–2): 229–35. doi:10.1007/s002210050842.

Matosin, Natalie, Elisabeth Frank, Martin Engel, Jeremy S Lum, and Kelly a Newell. 2014. "Negativity towards Negative Results: A Discussion of the Disconnect between Scientific Worth

and Scientific Culture." *Disease Models & Mechanisms* 7 (2): 171–73. doi:10.1242/dmm.015123.

Mc Cabe, Sofía I, Jorge Ignacio Villalta, Ghislain Saunier, Scott T Grafton, and Valeria Della-Maggiore. 2014. "The Relative Influence of Goal and Kinematics on Corticospinal Excitability Depends on the Information Provided to the Observer." *Cerebral Cortex (New York, N.Y. : 1991)*, no. Experiment 3: 2229–37. doi:10.1093/cercor/bhu029.

McNeill, D. 2000. *Language and Gesture*.

Mervis, Jeffrey. 2014. "Why Null Results Rarely See the Light of Day." *Science* 345 (6200): 992. doi:doi: 10.1126/science.345.6200.992.

Mills, K. 1999. *Magnetic Stimulation of the Humans Nervous System*. Oxford Uni. Oxford.

Miniussi, Carlo, Justin A. Harris, and Manuela Ruzzoli. 2013. "Modelling Non-Invasive Brain Stimulation in Cognitive Neuroscience." *Neuroscience and Biobehavioral Reviews* 37 (8). Elsevier Ltd: 1702–12. doi:10.1016/j.neubiorev.2013.06.014.

Molenberghs, P, R Cunnington, and J B Mattingley. 2012. "Brain Regions with Mirror Properties: A Meta Analysis of 125 Human FMRI Studies." *Neuroscience and Biobehavioral Reviews* 36 (1): 341–49. doi:http://dx.doi.org/10.1016/.

Montepare, Joann M, Sabra B Goldstein, and Annmarie Clausen. 1987. "The Identification of Emotions from Gait." *Journal of Nonverbal Behavior* 11 (1): 33. doi:10.1016/j.scijus.2016.05.006.

Münte, Thomas F, Eckart Altenmüller, and Lutz Jäncke. 2002. "The Musician's Brain as a Model of Neuroplasticity." *Nature Reviews Neuroscience* 3 (6): 473–78. doi:10.1038/nrn843.

Murakami, Takenobu, Julia Restle, and Ulf Ziemann. 2011. "Observation-Execution Matching and Action Inhibition in Human Primary Motor Cortex during Viewing of Speech-Related Lip Movements or Listening to Speech." *Neuropsychologia* 49 (7): 2045–54. doi:10.1016/j.neuropsychologia.2011.03.034.

Naish, Katherine R., Carmel Houston-Price, Andrew J. Bremner, and Nicholas P. Holmes. 2014. "Effects of Action Observation on Corticospinal Excitability: Muscle Specificity, Direction, and Timing of the Mirror Response." *Neuropsychologia* 64 (November). Elsevier: 331–48. doi:10.1016/j.neuropsychologia.2014.09.034.

Nakamura, H, H Kitagawa, Y Kawaguchi, and H Tsuji. 1997. "Intracortical Facilitation and Inhibition after Transcranial Magnetic Stimulation in Conscious Humans." *The Journal of Physiology* 498 (3). doi:https://doi.org/10.1113/jphysiol.1997.sp021905.

Neubert, Franz Xaver, Rogier B. Mars, Etienne Olivier, and Matthew F S Rushworth. 2011. "Modulation of Short Intra-Cortical Inhibition during Action Reprogramming." *Experimental*

Brain Research 211 (2): 265–76. doi:10.1007/s00221-011-2682-3.

Newman-Norlund, Roger D, Matthijs L Noordzij, Ruud Meulenbroek, and Harold Bekkering. 2007. "Exploring the Brain Basis of Joint Action: Co-Ordination of Actions, Goals and Intentions." *Social Neuroscience* 2 (1).

Newman-Norlund, Roger D, Hein T van Schie, Alexander M J van Zuijlen, and Harold Bekkering. 2007. "The Mirror Neuron System Is More Active during Complementary Compared with Imitative Action." *Nature Neuroscience* 10 (7): 817–18. doi:10.1038/nn1911.

Ng, Tommy H.B., Paul F. Sowman, Jon Brock, and Blake W. Johnson. 2013. "Neuromagnetic Brain Activity Associated with Anticipatory Postural Adjustments for Bimanual Load Lifting." *NeuroImage* 66. Elsevier Inc.: 343–52. doi:10.1016/j.neuroimage.2012.10.042.

Nichols, T E, and Andrew P Holmes. 2001. "Nonparametric Permutation Tests for Functional Neuroimaging Experiments: A Primer with Examples." *Human Brain Mapping* 15 (1): 1–25. doi:10.1002/hbm.1058.

Nielsen, Jens Bo. 2016. "Human Spinal Motor Control." *Annual Review of Neuroscience* 39 (1): annurev-neuro-070815-013913. doi:10.1146/annurev-neuro-070815-013913.

Nieuwenhuis, Sander, Clay B. Holroyd, Nisan Mol, and Michael G.H. Coles. 2004. "Reinforcement-Related Brain Potentials from Medial Frontal Cortex: Origins and Functional Significance." *Neuroscience and Biobehavioral Reviews* 28 (4): 441–48. doi:10.1016/j.neubiorev.2004.05.003.

Nirkko, A. C., K. M. Rösler, C. Ozdoba, O. Heid, G. Schroth, and C. W. Hess. 1997. "Human Cortical Plasticity: Functional Recovery with Mirror Movements." *Neurology* 48 (4): 1090–93. doi:10.1212/WNL.48.4.1090.

Novembre, Giacomo, Luca F. Ticini, Simone Schütz-Bosbach, and Peter E. Keller. 2014. "Motor Simulation and the Coordination of Self and Other in Real-Time Joint Action." *Social Cognitive and Affective Neuroscience* 9 (8): 1062–68. doi:10.1093/scan/nst086.

Oldfield, R.C. 1971. "The Assessment And Analysis Of Handedness: The Edinburgh Inventory." *Neuropsychologia* 9 (1): 97–113.

Oullier, Olivier, Gonzalo C De Guzman, Kelly J Jantzen, Julien Lagarde, and Scott Kelso. 2008. "Social Coordination Dynamics : Measuring Human Bonding." *Soc Neurosci.* 3 (2): 178–92.

Paizis, Christos, Charalambos Papaxanthis, Bastien Berret, and Thierry Pozzo. 2008. "Reaching Beyond Arm Length in Normal Aging : Adaptation of Hand Trajectory and Dynamic Equilibrium." *Behavioral Neuroscience* 122 (6): 1361–70. doi:10.1037/a0013280.

Palmer, C E, K L Bunday, M Davare, and James M Kilner. 2016. "A Causal Role for Primary Motor Cortex in Perception of Observed Actions." *Journal of Cognitive Neuroscience*, 1–9. doi:10.1162/jocn_a_01015.

Pantazis, Dimitrios, Thomas E. Nichols, Sylvain Baillet, and Richard M. Leahy. 2005. "A Comparison of Random Field Theory and Permutation Methods for the Statistical Analysis of MEG Data." *NeuroImage* 25 (2): 383–94. doi:10.1016/j.neuroimage.2004.09.040.

Patuzzo, Simone, Antonio Fiaschi, and Paolo Manganotti. 2003. "Modulation of Motor Cortex Excitability in the Left Hemisphere during Action Observation: A Single- and Paired-Pulse Transcranial Magnetic Stimulation Study of Self- and Non-Self-Action Observation." *Neuropsychologia* 41: 1272–78. doi:10.1002/1097-0142(196302)16:2<195::AID-CNCR2820160208>3.0.CO;2-7.

Perrig, S., O. Kazennikov, and M. Wiesendanger. 1999. "Time Structure of a Goal-Directed Bimanual Skill and Its Dependence on Task Constraints." *Behavioural Brain Research* 103 (1): 95–104. doi:10.1016/S0166-4328(99)00026-1.

Pezzulo, Giovanni, Francesco Donnarumma, Haris Dindo, Alessandro D'Ausilio, Ivana Konvalinka, and Cristiano Castelfranchi. 2018. "The Body Talks: Sensorimotor Communication and Its Brain and Kinematic Signatures." *Physics of Life Reviews*, no. June. doi:10.1016/j.plrev.2018.06.014.

Pezzulo, Giovanni, Pierpaolo Iodice, Francesco Donnarumma, Haris Dindo, and Günther Knoblich. 2017. "Avoiding Accidents at the Champagne Reception: A Study of Joint Lifting and Balancing." *Psychological Science* 28 (3): 338–45. doi:10.1177/0956797616683015.

Pineda, Jaime A. 2008. "Sensorimotor Cortex as a Critical Component of an 'extended' Mirror Neuron System: Does It Solve the Development, Correspondence, and Control Problems in Mirroring?" *Behavioral and Brain Functions* 4: 1–16. doi:10.1186/1744-9081-4-47.

Pistohl, Tobias, Andreas Schulze-Bonhage, Ad Aertsen, Carsten Mehring, and Tonio Ball. 2012. "Decoding Natural Grasp Types from Human ECoG." *NeuroImage* 59 (1). Elsevier Inc.: 248–60. doi:10.1016/j.neuroimage.2011.06.084.

Poggi, I. 2011. "Music and Leadership, the Choir Conductor's Multimodal Communication." *Integrating Gestures*, 341–53.

Porter, R., and R. N. Lemon. 1993. *Corticospinal Function and Voluntary Movement*. Oxford Uni. USA: Oxford University Press.

Posner, Michael I. 1980. "Orienting of Attention." *Quarterly Journal of Experimental Psychology* 32 (1): 3–25. doi:10.1080/00335558008248231.

Pozzo, Thierry, Mourad Ouamer, and Christian Gentil. 2001. "Simulating Mechanical Consequences of Voluntary Movement upon Whole-Body Equilibrium: The Arm-Raising Paradigm Revisited." *Biological Cybernetics* 85 (1): 39–49. doi:10.1007/PL00007995.

Ramnani, Narender, and R. Christopher Miall. 2004. "A System in the Human Brain for Predicting

the Actions of Others." *Nature Neuroscience* 7 (1): 85–90. doi:10.1038/nn1168.

Rand, Miya K., Martin Lemay, Linda M. Squire, Yury P. Shimansky, and George E. Stelmach. 2007. "Role of Vision in Aperture Closure Control during Reach-to-Grasp Movements." *Experimental Brain Research* 181 (3): 447–60. doi:10.1007/s00221-007-0945-9.

Repp, B H. 2005. "Sensorimotor Synchronisation; a Review of the Tapping Litterature." *Pschonomic Bulletin & Review* 12 (6): 969–92.

Reynolds, Charlene, and Peter Ashby. 1999. "Inhibition in the Human Motor Cortex Is Reduced Just before a Voluntary Contraction." *Neurology* 53 (4). doi:https://doi.org/10.1212/WNL.53.4.730.

Richardson, Michael J., Kerry L. Marsh, Robert W. Isenhower, Justin R.L. Goodman, and R. C. Schmidt. 2007. "Rocking Together: Dynamics of Intentional and Unintentional Interpersonal Coordination." *Human Movement Science* 26 (6): 867–91. doi:10.1016/j.humov.2007.07.002.

Ridding, Michael C, and Ulf Ziemann. 2010. "Determinants of the Induction of Cortical Plasticity by Non-Invasive Brain Stimulation in Healthy Subjects." *The Journal of Physiology* 588 (13): 2291–2304. doi:10.1113/jphysiol.2010.190314.

Rizzolatti, Giacomo, R. Camarda, Leonardo Fogassi, Maurizio Gentilucci, G. Luppino, and M. Matelli. 1988. "Functional Organization of Inferior Area 6 in the Macaque Monkey - I. Somatotopy and the Control of Proximal Movements." *Experimental Brain Research* 71: 491–507. doi:10.1007/BF00248741.

Rizzolatti, Giacomo, and Laila Craighero. 2004. "The Mirror-Neuron System." *Annual Review of Neuroscience* 27 (1): 169–92. doi:10.1146/annurev.neuro.27.070203.144230.

Rizzolatti, Giacomo, Leonardo Fogassi, and Vittorio Gallese. 2001. "Neurophysiological Mechanisms Underlying the Understanding and Imitation of Action." *Nature Reviews Neuroscience* 2 (September): 1–10. doi:10.1038/35090060.

Rizzolatti, Giacomo, and Corrado Sinigaglia. 2016. "The Mirror Mechanism: A Basic Principle of Brain Function." *Nature Reviews Neuroscience* 17 (12). Nature Publishing Group: 757–65. doi:10.1038/nrn.2016.135.

Romani, Michela, Paola Cesari, Cosimo Urgesi, Stefano Facchini, and Salvatore Maria Aglioti. 2005. "Motor Facilitation of the Human Cortico-Spinal System during Observation of Bio-Mechanically Impossible Movements." *NeuroImage* 26 (3): 755–63. doi:10.1016/j.neuroimage.2005.02.027.

Rossi, S., F. Tecchio, P. Pasqualetti, M. Ulivelli, V. Pizzella, G. L. Romani, S. Passero, N. Battistini, and P. M. Rossini. 2002. "Somatosensory Processing during Movement Observation in Humans." *Clinical Neurophysiology* 113 (1): 16–24. doi:10.1016/S1388-2457(01)00725-8.

Rossi, Simone, Mark Hallett, Paolo M. Rossini, and Alvaro Pascual-Leone. 2009. "Safety, Ethical

Considerations, and Application Guidelines for the Use of Transcranial Magnetic Stimulation in Clinical Practice and Research." *Clinical Neurophysiology* 120 (12): 2008–39. doi:10.1016/j.clinph.2009.08.016.

Rossini, P. M., A. T. Barker, A. Berardelli, M. D. Caramia, G. Caruso, G. Cracco, R. Q. Cracco, et al. 1994. "Non-Invasive Electrical and Magnetic Stimulation of the Brain, Spinal Cord and Roots: Basic Principles and Procedures for Routine Clinical Application." *Electroencephalography and Clinical Neurophysiology* 91 (2): 79–92.

Rossini, P. M., D. Burke, R. Chen, L. G. Cohen, Z. Daskalakis, R. Di Iorio, V. Di Lazzaro, et al. 2015. "Non-Invasive Electrical and Magnetic Stimulation of the Brain, Spinal Cord, Roots and Peripheral Nerves: Basic Principles and Procedures for Routine Clinical and Research Application: An Updated Report from an I.F.C.N. Committee." *Clinical Neurophysiology* 126 (6). International Federation of Clinical Neurophysiology: 1071–1107. doi:10.1016/j.clinph.2015.02.001.

Sacheli, Lucia Maria, Emmanuele Tidoni, Enea Francesco Pavone, Salvatore Maria Aglioti, and Matteo Candidi. 2013. "Kinematics Fingerprints of Leader and Follower Role-Taking during Cooperative Joint Actions." *Experimental Brain Research* 226 (4): 473–86. doi:10.1007/s00221-013-3459-7.

Santello, Marco, Gabriel Baud-Bovy, and Henrik Jörntell. 2013. "Neural Bases of Hand Synergies." *Frontiers in Computational Neuroscience* 7 (April): 23. doi:10.3389/fncom.2013.00023.

Sartori, Luisa, and Sonia Betti. 2015. "Complementary Actions." *Frontiers in Psychology* 6 (MAY): 1–6. doi:10.3389/fpsyg.2015.00557.

Sartori, Luisa, Sonia Betti, Eris Chinellato, and Umberto Castiello. 2015. "The Multiform Motor Cortical Output: Kinematic, Predictive and Response Coding." *Cortex* 70. Elsevier Ltd: 169–78. doi:10.1016/j.cortex.2015.01.019.

Schilbach, Leonhard, Bert Timmermans, Vasudevi Reddy, Alan Costall, Gary Bente, Tobias Schlicht, and Kai Vogeley. 2013. "Toward a Second-Person Neuroscience." *The Behavioral and Brain Sciences* 36: 393–414. doi:10.1017/S0140525X12000660.

Schmidt, Richard A, and T D Lee. 1999. *Motor Control and Learning: A Behavioral Approach*. Human Kine. Champaign, IL.

Schmidt, Richard A, and Douglas E Young. 1986. "Transfer of Movement Control in Motor Skill Training." In *Transfer of Learning*, edited by S M Cormier and J D Hagman. Orlando: Academic Press.

Schmidt, S., R. M. Cichy, A. Kraft, J. Brocke, K. Irlbacher, and S. A. Brandt. 2009. "Clinical Neurophysiology An Initial Transient-State and Reliable Measures of Corticospinal Excitability

in TMS Studies." *Clinical Neurophysiology* 120: 987–93. doi:10.1016/j.clinph.2009.02.164.

Schmitz, Judith, Eleonora Bartoli, Laura Maffongelli, Luciano Fadiga, Nuria Sebastian-Galles, and Alessandro D'Ausilio. 2018. "Motor Cortex Compensates for Lack of Sensory and Motor Experience during Auditory Speech Perception." *Neuropsychologia*, no. December 2017: 1–7. doi:10.1016/j.neuropsychologia.2018.01.006.

Sebanz, Natalie, Harold Bekkering, and G??nther Knoblich. 2006. "Joint Action: Bodies and Minds Moving Together." *Trends in Cognitive Sciences* 10 (2): 70–76. doi:10.1016/j.tics.2005.12.009.

Sebanz, Natalie, and Guenther Knoblich. 2009. "Prediction in Joint Action: What, When, and Where." *Topics in Cognitive Science* 1 (2): 353–67. doi:10.1111/j.1756-8765.2009.01024.x.

Sebanz, Natalie, and Maggie Shiffrar. 2009. "Detecting Deception in a Bluffing Body: The Role of Expertise." *Psychonomic Bulletin and Review* 16 (1): 170–75. doi:10.3758/PBR.16.1.170.

Senna, Irene, Nadia Bolognini, and Angelo Maravita. 2014. "Grasping with the Foot: Goal and Motor Expertise in Action Observation." *Human Brain Mapping* 35 (4): 1750–60. doi:10.1002/hbm.22289.

Senot, Patrice, Alessandro D'Ausilio, Michele Franca, Luana Caselli, Laila Craighero, and Luciano Fadiga. 2011. "Effect of Weight-Related Labels on Corticospinal Excitability during Observation of Grasping: A TMS Study." *Experimental Brain Research* 211 (1): 161–67. doi:10.1007/s00221-011-2635-x.

Serrien, Deborah J., and Mario Wiesendanger. 2000. "Temporal Control of a Bimanual Task in Patients with Cerebellar Dysfunction." *Neuropsychologia* 38 (5): 558–65. doi:10.1016/S0028-3932(99)00116-5.

Seth, Anil K. 2010. "A MATLAB Toolbox for Granger Causal Connectivity Analysis." *Journal of Neuroscience Methods* 186 (2): 262–73. doi:10.1016/j.jneumeth.2009.11.020.

Shimada, Sotaro, and Ryosuke Abe. 2009. "Modulation of the Motor Area Activity during Observation of a Competitive Game." *NeuroReport* 20 (11): 979–83. doi:10.1097/WNR.0b013e32832d2d36.

———. 2010. "Outcome and View of the Player Modulate Motor Area Activity during Observation of a Competitive Game." *Neuropsychologia* 48 (7): 1930–34. doi:10.1016/j.neuropsychologia.2010.03.012.

Singh, Krish D., Gareth R. Barnes, and Arjan Hillebrand. 2003. "Group Imaging of Task-Related Changes in Cortical Synchronisation Using Nonparametric Permutation Testing." *NeuroImage* 19 (4): 1589–1601. doi:10.1016/S1053-8119(03)00249-0.

Sitnikova, Tatiana, Phillip J. Holcomb, Kristi A. Kiyonaga, and Gina R. Kuperberg. 2008. "Two Neurocognitive Mechanisms of Semantic Integration during the Comprehension of Visual Real-

World Events." *Journal of Cognitive Neuroscience* 20 (11): 2037–57. doi:10.1162/jocn.2008.20143.

Slowiński, Piotr, Francesco Alderisio, Chao Zhai, Yuan Shen, Peter Tino, Catherine Bortolon, Delphine Capdevielle, et al. 2017. "Unravelling Socio-Motor Biomarkers in Schizophrenia." *Npj Schizophrenia* 3 (8). doi:10.1038/s41537-016-0009-x.

Słowiński, Piotr, Chao Zhai, Francesco Alderisio, Robin Salesse, Mathieu Gueugnon, Ludovic Marin, Benoit G. Bardy, et al. 2016. "Dynamic Similarity Promotes Interpersonal Coordination in Joint Action." *Journal of The Royal Society Interface* 13 (116): 20151093. doi:10.1098/rsif.2015.1093.

Sohn, Young H, Katy Wiltz, and Mark Hallett. 2002. "Effect of Volitional Inhibition on Cortical Inhibitory Mechanisms." *Journal of Neurophysiology* 88 (1): 333–38. doi:10.1152/jn.00863.2001.

Soriano, Marco, Andrea Cavallo, Alessandro D'Ausilio, Cristina Becchio, and Luciano Fadiga. 2018. "Movement Kinematics Drive Chain Selection toward Intention Detection." *Proceedings of the National Academy of Sciences of the United States of America*. doi:https://doi.org/10.1073/pnas.1809825115.

Sporns, O, and G M Edelman. 1993. "Solving Bernstein's Problem: A Proposal for the Development of Coordinated Movement by Selection." *Child Development* 64 (4): 960–81. doi:10.1111/j.1467-8624.1993.tb04182.x.

Stapel, Janny C, Sabine Hunnius, Michiel van Elk, and Harold Bekkering. 2010. "Motor Activation during Observation of Unusual versus Ordinary Actions in Infancy." *Social Neuroscience* 5 (5–6): 451–60. doi:https://doi.org/10.1080/17470919.2010.490667.

Stapley, Paul, Thierry Pozzo, Guy Cheron, and Alexander Grishin. 1999. "Does the Coordination between Posture and Movement during Human Whole-Body Reaching Ensure Center of Mass Stabilization?" *Experimental Brain Research* 129 (1): 134–46. http://www.ncbi.nlm.nih.gov/pubmed/10550511.

Stapley, Paul, Thierry Pozzo, and Alexander Grishin. 1998. "The Role of Anticipatory Postural Adjustments during Whole Body Forward Reaching Movements." *Neuroreport* 9 (3): 395–401. doi:10.1097/00001756-199802160-00007.

Stefan, Katja, Joseph Classen, Pablo Celnik, and Leonardo G. Cohen. 2008. "Concurrent Action Observation Modulates Practice-Induced Motor Memory Formation." *European Journal of Neuroscience* 27 (3): 730–38. doi:10.1111/j.1460-9568.2008.06035.x.

Stefan, Katja, Leonardo G. Cohen, Julie Duque, Riccardo Mazzocchio, Pablo Celnik, Lumy Sawaki, Leslie Ungerleider, and Joseph Classen. 2005. "Formation of a Motor Memory by Action

Observation." *The Journal of Neuroscience* 25 (41): 9339–46. doi:10.1523/JNEUROSCI.2282-05.2005.

Stinear, Cathy M, and Winston D Byblow. 2003. "Role of Intracortical Inhibition in Selective Hand Muscle Activation." *Journal of Neurophysiology* 89: 2014–20. doi:10.1152/jn.00925.2002.

Strafella, AP, and T Paus. 2000. "Modulation of Cortical Excitability during Action Observation: A Transcranial Magnetic Stimulation Study." *Neuroreport* 11 (10): 2289–92.

Summerfield, Christopher, Tobias Egner, Matthew Greene, Etienne Koechlin, Jennifer Mangels, and Joy Hirsch. 2006. "Predictive Codes for Forthcoming Perception in the Frontal Cortex." *Molecular Biology of the Cell* 314: 1311–14. doi:10.1126/science.1132028.

Summerfield, Christopher, Tobias Egner, W. James, M.I. Posner, et al., M. Bar, U. Polat, et al. 2009. "Expectation (and Attention) in Visual Cognition." *Trends in Cognitive Sciences* 13 (9). Elsevier: 403–9. doi:10.1016/j.tics.2009.06.003.

Talmi, D., R. Atkinson, and W. El-Deredy. 2013. "The Feedback-Related Negativity Signals Salience Prediction Errors, Not Reward Prediction Errors." *Journal of Neuroscience* 33 (19): 8264–69. doi:10.1523/JNEUROSCI.5695-12.2013.

Tandonnet, C., M.I. Garry, and J.J. Summers. 2010. "Cortical Activation during Temporal Preparation Assessed by Transcranial Magnetic Stimulation." *Biological Psychology* 85 (3): 481–86. doi:10.1016/j.biopsycho.2010.08.016.

Thoroughman, Kurt A, and R Shadmehr. 2000. "Learning of Action through Adaptative Combination of Motor Primitives." *Nature* 407 (6805): 742–47. doi:10.1038/35037588.Learning.

Thoroughman, Kurt A, and Reza Shadmehr. 1999. "Electromyographic Correlates of Learning an Internal Model of Reaching Movements." *The Journal of Neuroscience* 19 (19): 8573–88. doi:10.1203/01.pdr.0000176834.47305.26.

Tkach, Dennis, Jacob Reimer, and Nicholas G Hatsopoulos. 2007. "Congruent Activity during Action and Action Observation in Motor Cortex." *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience* 27 (48): 13241–50. doi:10.1523/JNEUROSCI.2895-07.2007.

Urgen, Burcu A, and Luke E Miller. 2015. "Towards an Empirically Grounded Predictive Coding Account of Action Understanding." *The Journal of Neuroscience* 35 (12): 4789–91. doi:10.1523/JNEUROSCI.0144-15.2015.

Urgesi, Cosimo, Matteo Candidi, Franco Fabbro, Michela Romani, and Salvatore M. Aglioti. 2006. "Motor Facilitation during Action Observation: Topographic Mapping of the Target Muscle and Influence of the Onlooker's Posture." *European Journal of Neuroscience* 23 (9): 2522–30. doi:10.1111/j.1460-9568.2006.04772.x.

Urgesi, Cosimo, Marta Maieron, Alessio Avenanti, Emmanuele Tidoni, Franco Fabbro, and Salvatore

Maria Aglioti. 2010. "Simulating the Future of Actions in the Human Corticospinal System." *Cerebral Cortex* 20 (11): 2511–21. doi:10.1093/cercor/bhp292.

Vallence, A. M., M. R. Goldsworthy, N. A. Hodyl, J. G. Semmler, J. B. Pitcher, and M. C. Ridding. 2015. "Inter- and Intra-Subject Variability of Motor Cortex Plasticity Following Continuous Theta-Burst Stimulation." *Neuroscience* 304. IBRO: 266–78. doi:10.1016/j.neuroscience.2015.07.043.

van Schie, Hein T., Rogier B. Mars, Michael G.H. H Coles, and Harold Bekkering. 2004. "Modulation of Activity in Medial Frontal and Motor Cortices during Error Observation." *Nature Neuroscience* 7 (5): 549–54. doi:10.1038/nn1239.

van Ulzen, Niek R., Claudine J C Lamoth, Andreas Daffertshofer, Gün R. Semin, and Peter J. Beek. 2008. "Characteristics of Instructed and Uninstructed Interpersonal Coordination While Walking Side-by-Side." *Neuroscience Letters* 432 (2): 88–93. doi:10.1016/j.neulet.2007.11.070.

Vastano, Roberta, Alberto Inuggi, Claudia D. Vargas, Gabriel Baud-Bovy, Marco Jacono, and Thierry Pozzo. 2016. "Tactile Perception during Action Observation." *Experimental Brain Research* 234 (9): 2585–94. doi:10.1007/s00221-016-4663-z.

Vernet, Marine, Shahid Bashir, Woo-Kyoung Yoo, Lindsay Oberman, Ilan Mizrahi, Frederick Ifert-Miller, Charles J Beck, and Alvaro Pascual-Leone. 2014. "Reproducibility of the Effects of Theta Burst Stimulation on Motor Cortical Plasticity in Healthy Participants." *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology* 125 (2): 320–26. doi:10.1016/j.clinph.2013.07.004.

Vesper, Cordula, Stephen Butterfill, Günther Knoblich, and Natalie Sebanz. 2010. "A Minimal Architecture for Joint Action." *Neural Networks* 23 (8–9). Elsevier Ltd: 998–1003. doi:10.1016/j.neunet.2010.06.002.

Vesper, Cordula, Robrecht P R D Van Der Wel, Günther Knoblich, and Natalie Sebanz. 2011. "Making Oneself Predictable: Reduced Temporal Variability Facilitates Joint Action Coordination." *Experimental Brain Research* 211: 517–30. doi:10.1007/s00221-011-2706-z.

Viallet, F., J. Massion, R. Massarino, and R. Khalil. 1992. "Coordination between Posture and Movement in a Bimanual Load Lifting Task: Putative Role of a Medial Frontal Region Including the Supplementary Motor Area." *Experimental Brain Research* 88 (3): 674–84. doi:10.1007/BF00228197.

Võ, Melissa L-H, and Jeremy M Wolfe. 2013. "Differential Electrophysiological Signatures of Semantic and Syntactic Scene Processing." *Psychological Science* 24 (9). SAGE Publications: 1816–23. doi:10.1177/0956797613476955.

Volpe, Gualtiero, P Alborno, Antonio Camurri, Paolo Coletta, S Ghisio, M Mancini, R

Niewiadomski, and Stefano Piana. 2016. "Designing Multimodal Interactive Systems Using Eyesweb Xmi." In *Proceedings of the First International Workshop on Smart Ecosystems CReation by Visual Design Co-Located with the International Working Conference on Advanced Visual Interfaces*, 49–56.

Volpe, Gualtiero, Alessandro D'Ausilio, Leonardo Badino, Antonio Camurri, and Luciano Fadiga. 2016. "Measuring Social Interaction in Music Ensembles." *Philosophical Transactions B* 371 (April): 20150377. doi:10.1098/rstb.2015.0377.

Wanderley, Marcelo M. 2002. "Quantitative Analysis of Non-Obvious Performer Gestures." In *Proc. Gesture Workshop 2001*, 241–53. doi:10.1007/3-540-47873-6_26.

Wang, Chunmao, Istvan Ulbert, Dolnald L Schomer, Ksenija Marinkovic, and Eric Halgren. 2005. "Responses of Human Anterior Cingulate Cortex Microdomains to Error Detection, Conflict Monitoring, Stimulus-Response Mapping, Familiarity, and Orienting." *The Journal of Neuroscience* 25 (3): 604–13. doi:10.1523/JNEUROSCI.4151-04.2005.

Welch, B L. 1947. "The Generalization of 'Student's' Problem When Several Different Population Variances Are Involved." *Biometrika* 34 (1–2): 28–35.

Wessel, Jan R., and Adam R. Aron. 2017. "On the Globality of Motor Suppression: Unexpected Events and Their Influence on Behavior and Cognition." *Neuron*. doi:10.1016/j.neuron.2016.12.013.

Westfall, Peter H, and Stanley S Young. 1993. *Resampling-Based Multiple Testing:* Wiley. New-York. doi:10.2307/1270279.

Wiesendanger, Mario, Oleg Kazennikov, Stephen Perrig, and Pawel Kaluzny. 1996. "Two Hands—one Action: The Problem of Bimanual Coordination." In *Hand and Brain: The Neurophysiology and Psychology of Hand Movements*, edited by Alan M Wing, Patrick Haggard, and J Randall Flanagan, 283–300. San Diega, CA, US: Academic Press.

Wiesendanger, Mario, and Deborah J Serrien. 2004. "The Quest to Understand Bimanual Coordination." *Progress in Brain Research* 143: 491–505. doi:10.1016/S0079-6123(03)43046-X.

Williams, A, and Paul L Gribble. 2012. "Observed Effector-Independent Motor Learning by Observing." *J Neurophysiol* 107 (6): 1564–70. doi:10.1152/jn.00748.2011.

Wilson, Margaret, and Günther Knoblich. 2005. "The Case for Motor Involvement in Perceiving Conspecifics." *Psychological Bulletin* 131 (3): 460–73. doi:10.1037/0033-2909.131.3.460.

Witney, A G, S J Goodbody, and D M Wolpert. 1999. "Predictive Motor Learning of Temporal Delays." *Journal of Neurophysiology* 82 (5): 2039–48. doi:10.1152/jn.1999.82.5.2039.

Wöllner, Clemens. 2008. "Which Part of the Conductor's Body Conveys Most Expressive

Information? A Spatial Occlusion Approach." *Musicae Scientiae* 12 (2): 249–72. doi:10.1177/102986490801200204.

Wolpert, Daniel M. 1997. "Computational Approaches to Motor Control." *Trends in Cognitive Sciences* 1 (6): 209–16. doi:10.1016/S1364-6613(97)01070-X.

Wolpert, Daniel M, Kenji Doya, and Mitsuo Kawato. 2003. "A Unifying Computational Framework for Motor Control and Social Interaction." *Philosophical Transactions of the Royal Society of London* 358 (February): 593–602. doi:10.1098/rstb.2002.1238.

Zatorre, Robert J., Joyce L. Chen, and Virginia B. Penhune. 2007. "When the Brain Plays Music: Auditory-Motor Interactions in Music Perception and Production." *Nature Reviews. Neuroscience* 8 (7): 547–58. doi:10.1038/nrn2152.

Ziemann, Ulf. 2004. "TMS and Drugs." *Clinical Neurophysiology* 115 (8): 1717–29. doi:10.1016/j.clinph.2004.03.006.

Ziemann, Ulf, Silke Lönnecker, Bernhard J. Steinhoff, and Walter Paulus. 1996. "The Effect of Lorazepam on the Motor Cortical Excitability in Man." *Experimental Brain Research* 109 (1): 127–35. doi:10.1007/BF00228633.

Ziemann, Ulf, John C Rothwell, and Michael C Ridding. 1996. "Interaction between Intracortical Inhibition and Facilitation in Human Motor Cortex." *The Journal of Physiology* 496 (3).

Ziemann, Ulf, Frithjof Tergau, Eric M Wassermann, Stephan Wischer, Jorg Hildebrandt, and Walter Paulus. 2004. "Demonstration of Facilitatory I Wave Interaction in the Human Motor Cortex by Paired Transcranial Magnetic Stimulation." *The Journal of Physiology* 511 (1). doi:https://doi.org/10.1111/j.1469-7793.1998.181bi.x.