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Brain Asymmetries

The lateralization of three different cognitive processes

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Abstract

The hemispheric lateralization has received attention across years because its implication in determine behavioural and individual differences. Specifically, the left hemisphere's expansion and specialization in the course of the evolution received a lot of attention for its involvement in language functioning. Nevertheless, also the right hemisphere expanded and, in particular, the right parietal lobe increased its dimension and its connections, becoming a specialized area for the multisensory integration mechanisms. Even if the parietal lobe has been extensively studied, there are still unanswered questions about the lateralization of different cognitive processes related to this area.

Given the broad implication of the parietal areas in several cognitive processes, in this thesis three stand-alone studies on healthy population are presented. The studies are independent even if all of them aim at exploring the lateralization of cognitive processes typically related to the parietal areas. A hierarchical structure was followed from the most basic to the most complex cognitive process: (i) visuo-spatial attention, (ii) motor behaviour and (iii) body representation.

In the first study, thirty-six right- and left-handers participants were tested during perceptual (Line Bisection) and representational (Mental Number Line) tasks. Taking into consideration the attentional bias (pseudoneglect), results showed a greater difference between the perceptual and representational domains in the left-handers group. This difference is led by a bias farther to the left in the representational domain, but not in the perceptual one, compared to right-handers. These results suggest that right- and left-handers are differently affected by attentional asymmetries depending on the domain being representational or perceptual.

The second study aimed at exploring the lateralization of the bimanual temporal coupling effect. Thirty-two participants were tested during a bimanual task while the transcranial Direct Current Stimulation was applied over right and left parietal area. Results highlight different effects of the stimulation depending on the level of complexity of the movement.

In the third study, eighteen participants were tested during implicit (not requiring awareness) and explicit (requiring awareness) body-schema related tasks while a cathodic or sham transcranial Direct Current Stimulation was delivered on the right parietal area. Results highlight an effect of stimulation specific for the implicit task, and selective for identification processes rather than widespread to motor related aspects. These results challenge the general idea of a right hemispheric dominance, and rather suggest that body schema processes rely on a bilateral network dependent on awareness encompassing both the left and the right hemisphere.

The three studies together highlight that a black or white hemispheric lateralization of cognitive processes related to parietal areas is not feasible at this point. Indeed, specific features (domain, complexity and awareness) play an important role in concluding for a right or left dominance. For this reason, future studies are needed in order to clarify their weight using different techniques together.

Chapter 1

General introduction

1. The cerebral lateralization

With lateralization, it is usually indicated the specialization of one hemisphere than the other in leading a specific cognitive ability. For instance, although reductive, it is well-known the role of the left hemisphere for language abilities (Broca, 1865) and the role of the right one for visuo-spatial abilities (Newcombe and Ratcliff, 1989).

Several theories discussed the role of the lateralization in the evolutionary framework agreeing on the fact that lateralization could be useful in terms of neural efficiency (Rogers, Vallortigara, & Andrew, 2013): neural tissue is saved avoiding duplication of the same functions in both hemispheres. However, this possible advantage is counterbalanced by the disadvantage in case of unilateral brain lesions after which the lost function is no more recoverable by the structures of the other hemisphere (Rogers et al., 2013). Another hypothesis supports the vision of the lateralization for the parallel processing within the two hemispheres separately (Rogers, Zucca, & Vallortigara, 2004). In summary, independently from the reference theory, the brain lateralization seems to be a convenient condition for the cerebral efficiency (Rogers et al., 2013).

If it is clear the role of the lateralization at an individual level, more debatable is the role of the lateralization at a population level. Each individual is lateralized (e.g. right *vs* left dominant hand) but the majority of the population manifest a specific directionality (e.g. right dominant hand in 90% of the human population). Even in this case, there are some theories that tried to explain that directionality. For instance, McManus suggested the role of the genes in determining left-right differences in body and brain structures (McManus, 2002). Some other theories hypothesize a socio-cultural origin of the lateralization (McManus, 2002). Accordingly, it is possible to postulate that the majority of human beings are right-handers because objects and artefacts are built with an intrinsic advantage for right- than left-handers. However, this could be a consequence rather than the cause of the lateralization (Rogers et al., 2013). An alternative theory suggested the existence of social bond responsible for the alignment of individual asymmetries to those manifested by the group (Vallortigara & Rogers, 2005). This theory is founded on the concept of "evolutionary stable strategy" (Ray-Mukherjee & Mukherjee, 2016): each lateralized individual started to align his lateralization' directionality on the basis of other individuals' asymmetries. This could be happened when such asymmetries became relevant during the evolution for the interactions between individuals (Ghirlanda & Vallortigara, 2004; Vallortigara & Rogers, 2005). Consequently, the advantage for an individual will depend by his success in those interactions (Rogers et al., 2013).

Regardless these theories, what it is worth to highlight is that behavioural asymmetries correspond to cerebral asymmetries. Right and left hemisphere are well-defined in their functions not only in human population, providing evidence for the evolutionary significance of lateralization. Such evidence, derived from studies on other species like dogs, birds and apes, show that the left hemisphere is devoted to approach mechanisms and positive emotions while the right hemisphere is related with avoidance mechanisms and negative emotions (Bonati, Csermely, & Romani, 2008; de Latude, Demange, Bec, & Blois-Heulin, 2009; Ehrlichman, 1987; Hopkins & Bennett, 1994; Lane & Jennings, 1995; Quaranta, Siniscalchi, & Vallortigara, 2007). In support of a hemispheric specialization in other species than humans, a study showed how the presentation of stimuli in the left or right hemi-field elicited different behavioural patterns in apes as well as in humans (Fagot & Deruelle, 1997). In this study, it was required to associate a stimulus letter (e.g. letter H composed by small letters A) with a target letter (e.g. letter A or H). When the stimulus letter was briefly shown in the right hemi-field (processed by left hemisphere), the local information (small letters A which composed the stimulus letter H) was used to solve the task. Conversely, when the same stimulus was shown in the left hemi-field (right hemisphere) the global information (big letter H) was used to solve the task (Fagot & Deruelle, 1997). This attested how the right and left hemispheres are clearly specialized in humans as well as in apes.

Focusing on the human population, evidence of lateralized cognition at an individual level derives historically from two different fields: the study of behavioural differences in case of experimental manipulation, as the brief presentation of stimuli in the right or left hemi-field while reaction times are recorded (Bradshaw, 1991), and the study of brain damaged patients. In this latter case, it is studied the effect of a unilateral lesion on the behaviour. This is what happens, for instance, in the study of hemispatial neglect in which patients manifest a shift towards the right side of the space following right hemisphere lesions (Driver & Mattingley, 1998; Mesulam, 1981) or in case of aphasia in which patients manifest a selective language impairment after left-hemisphere lesions (Broca, 1865). To date, other instruments can be used in order to compare the role of the right and left hemisphere in a specific cognitive ability. For instance, the use of neuromodulatory techniques, such as transcranial Direct Current Stimulation (tDCS) or Transcranial Magnetic Stimulation (TMS), represent a promising tool because they allow to interfere with the brain activity in specific regions avoiding the confounding variables related to bilateral effects in case of unilateral lesion. Furthermore, comparing the performance of differently lateralized population (e.g. right- *vs* left-handers) may represent another easy way to shed light on different lateralized behaviours.

Regarding the differences in right and left hemispheres in humans, a large amount of studies focused on the specialization during the evolution of the left hemisphere and, above all, on the role of the frontal areas for language and executive processes (Sherwood, Broadfield, Holloway, Gannon, & Hof, 2003; Spocter et al., 2010). It is less known that also the parietal lobe encountered similar changes in the course of the evolution (Aversi-ferreira, Ferreira, & Araújo, 2010). Furthermore, the right hemisphere could be considered as important as the left one because it is connected with more extensive areas and it is more specialized for the integration processes than the left one (Iturria-Medina et al., 2011).

In what follows, the focus will be on the parietal lobe as this area has a pivotal role in the integration of multimodal information such as somatosensory, visual and auditory information (Aversi-ferreira et al., 2010; Caspers et al., 2006). Without the functions related to this area, we could not be able to perform actions in the environment in a proper way, as it happens for example in case of apraxia following brain damages (Heilman, Rothi, & Valenstein, 1982) in which patients are no more able to perform the correct movements to reach the goal. In particular, the role of the right parietal lobe will be discussed because it is of uttermost importance allowing the interaction with the outside world (Aversi-ferreira et al., 2010).

2. The role of the Parietal Cortex

The parietal lobe is located between the frontal and the occipital lobe and it can be functionally divided into two main areas: anterior (which corresponds to the somatosensory cortex) and posterior (Posterior Parietal Cortex: PPC). In this latter region, particular attention is addressed to area PG in von Encomo’s map (area 39 in Brodmann’s classification). This area is not found in the monkey’ brain (Aversi-ferreira et al., 2010) and, during the course of the evolution, it expanded asymmetrically in humans (Kolb, & Whishaw, 2009). Such asymmetry reveals a larger area on the right than on the left of the human brain, suggesting a specialization related to visuo-spatial functioning (Kolb, & Whishaw, 2009). Furthermore, the visuo-spatial specialization of the PPC has been hypothesized because it is located between the visual and the somatosensory cortex, so that it receives both visual and somatosensory inputs (Culham, Cavina-Pratesi, & Singhal, 2006). The outputs deriving from here are sent principally to the frontal areas involving premotor and motor regions. For these reasons, the PPC is considered as a multisensory integration area (Culham et al., 2006).

The involvement of the PPC is widely described in association to several cognitive processes, apparently very distant from each other. Two examples are given by reaching actions and arithmetic processes. Specifically, it is well known the role of the PPC in reaching tasks used to assess the “where” pathway, as described by Goodale and Milner (Goodale & Milner, 1992). The authors identified two different visual streams, one related to the identification of what an object is (ventral stream) and the other one involved in the identification of where the object is (dorsal stream) (Goodale & Milner, 1992). The dorsal stream goes from the visual areas to the parietal area and it is of uttermost importance in order to guide actions in the space to interact with objects (Goodale & Milner, 1992). This attests clearly how the visuo-spatial information are integrated in a coherent visuo-spatial representation and how this information is “shared” with the motor areas in order to perform a correct movement in the space.

Another example of the PPC involvement derives from a different field: Dehaene et al. (2003) described the existence of three different parietal circuits involving in number processing. Specifically, the Intraparietal Sulcus would be involved in quantity processing because of a spatial representation of numerical quantity useful to perform, for instance, numbers comparison (Dehaene et al., 2003). The second circuit would involve the Angular Gyrus (AG) and it would be specific for verbal coding of numbers (Dehaene et al., 2003). The third circuit would include the Posterior Superior Parietal Lobule (PSPL) and it is active during counting (Piazza, Mechelli, Butterworth, & Price, 2002), subtraction (Lee, 2000) and approximation (Dehaene, Spelke, Pinel, Stanescu, & Tsivkin, 1999). However, this latter area does not seem to be specific for number processing as its involvement has been described also in reaching and spatial attentional tasks (Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000; Culham & Kanwisher, 2001).

Furthermore, the involvement of the PPC has been described in other domains such as working memory (LaBar, Gitelman, Parrish, & Mesulam, 1999), mental imagery (Pelgrims, Andres, & Olivier, 2009) and both auditory (Rao, Mayer, & Harrington, 2001) and visual (Battelli, Cavanagh, Martini, & Barton, 2003) analysis of time.

The Parietal Cortex (PC) is involved in so many different processes, as attested by these few examples, that it is worth to hypothesized that this area is responsible of multidimensional and more general processes rather than consider the PC a highly specialized area for each one of the above-mentioned process (Culham & Kanwisher, 2001). Probably, without the role of the PC some processes would not be performed correctly, as attested by impairments in case of parietal lesions. However, this does not mean that the PC is specialized for each one of those cognitive processes.

2.1 Lateralization of the Parietal Cortex

Evidence regarding the existence of a lateralization degree within the PC derives mainly from neuropsychological data of brain-damaged patients. For instance, it is well-established that impairments in visuo-spatial attention and visuo-spatial processing are more often related to right than left parietal lesions (Weintraub & Mesulam, 1987). The hemispatial neglect is one of the most representative case as it emerges most frequently after right hemisphere lesions (Gainotti, Messerli, & Tissot, 1972; Halligan, Fink, Marshall, & Vallar, 2003; Heilman, Watson, & Valenstein, 2003), even if cases of right hemispatial neglect have been described (Kleinman et al., 2007; Suchan, Rorden, & Karnath, 2012). Such specialization of the right PC for attention and visuo-spatial processing is also attested by neuroimaging studies that showed robustness in concluding for a pivotal role of the right side of the PC (Corbetta, Miezin, Shulman, & Petersen, 1993; Gitelman et al., 1999). However, left PC involvement has been described for attentional processes when verbal information is used (Shulman, d'Avossa, Tansy, & Corbetta, 2002).

A clear lateralization of PC is debated also taking into account the reach and grasp processing (Culham et al., 2006). A large body of studies attested a controlateral lateralization for reaching and grasping regarding the hand considered (Binkofski et al., 1998; Grafton et al., 1999; Karnath & Perenin, 2005), while others described a bilateral hemispheric involvement regardless the hand considered (Culham, Cavina Pratesi et al., 2004; Grefkes, Weiss, Zilles, & Fink, 2002). Hinkley et al. (2009), comparing the cortical activation related to three different tasks (saccadic eye movements; reach to grasp action; manual discrimination shape), highlighted a left hemispheric asymmetry for reaching and grasping processing (Hinkley, Krubitzer, Padberg, & Disbrow, 2009). Such asymmetry seems to be specific for visual-guided reaching-to-grasp actions since authors did not found the same asymmetric pattern of activation for the other task involving manual movements (manual discrimination shape) (Hinkley et al., 2009). A left hemispheric asymmetry for reaching-to-grasp actions was also found in one fMRI study by Chapman et al. (2002). In this study, participants were administered with reaching-to-grasp tasks that differed in complexity (different number of stimuli and different possible location of the stimuli). Regarding the task' complexity, the authors found an increase in the left Superior Parietal Lobule activation that could be explained in terms of motor attention demands associated with the limb preparation for movement (Chapman et al., 2002). To disentangle the possible confounding lateralized effect played by the hand considered (right hand related to the left hemisphere/left hand related to the right hemisphere), a study by Perenin and Vighetto (1998) on brain damaged patients suggested that the left parietal' damage affects both the controlateral hand as well as the controlateral hemi-field (Perenin & Vighetto, 1988). Conversely, right parietal damage affects only the controlateral hemi-field (Perenin & Vighetto, 1988). However, it is known from the literature that also a right parietal lesion can affect the controlateral hand (Culham et al., 2006).

A third process involving the PC, not clearly lateralised, is represented by the Body Representation (BR). BR is a complex process involving visuo-spatial representation, motor, sensory and proprioceptive information. Even if the debate about the classification of different body representations is out of matter here (see de Vignemont, 2010), the focus is on an action-oriented representation of the body involving multisensory integration (Holmes & Spence, 2004). A large body of evidence supports a right lateralization of this kind of BR. For instance, some studies described the same bias towards the left side of the space in spatial judgment of one's own body in right-handers but not in left-handers, as it happens in other visuo-perceptual tasks (e.g. line bisection) (Chokron, Colliot, Atzeni, Bartolomeo, & Ohlmann, 2004; Cocchini, Beschin, & Jehkonen, 2001; Hach & Schutz-Bosbach, 2010; Nicholls, Loftus, Mayer, & Mattingley, 2007). Furthermore, evidence for such right lateralization of the BR derives from brain damaged patients. As mentioned above, the hemispatial neglect is more frequent after right hemisphere lesions and this syndrome can affect BR, namely personal neglect (Bisiach, Perani, Vallar, & Berti, 1986; Committeri et al., 2007). Other bodily symptoms can emerge following right hemisphere lesions such as hemianesthesia in which patients do not perceive anymore tactile information from the controlesional side of the body (Sterzi et al., 1993) or somatoparaphrenia where patients manifest a sense of disownership for the controlesional limb (Bottini, Bisiach, Sterzi, & Vallar, 2002). Nevertheless, some studies described different phenomena involving the left hemisphere. It is the case of autotopoagnosia characterized by patients making errors in pointing and naming body parts (Semenza & Goodglass, 1985; Pick, 1992) or Gerstmann' syndrome where patients manifest fingers agnosia and left-right disorientation (Gerstmann, 1940).

In summary, while the classical studies tend to emphasize the role played by one hemisphere on the other in leading a specific cognitive ability, a clear-cut is difficult to prove. For instance, a meta-analysis highlights how it is difficult to conclude for a hemispheric dominance in visuo-spatial tasks without to consider all the variables that could affect the results (Vogel, Bowers, & Vogel, 2003). The authors discussed the role of moderator variables, like study types and assessment technique, in leading the conclusion of a dominant role of the right hemisphere in visuo-spatial tasks (Vogel et al., 2003).

Considering the various processes related to the PC, three different stand-alone studies are proposed here. The first presented study concerns the visuo-spatial attention in its perceptual and representational forms in two different lateralized populations, namely right- and left-handers. The second study aims at exploring the role of the right and left PC during bimanual tasks. Lastly, the third study is focused on the possible lateralization of BR components.

Chapter 2

Visuo-spatial attentional asymmetries in representational domain

1.Introduction

We need visuospatial abilities, which are strictly related to attentional ones, to successfully interact with the environment or to perform an action. Not by chance, a visuospatial bias can emerge when there is an impairment in attentional processes following a brain damage (Danckert & Ferber, 2006; Driver & Mattingley, 1998). The most significant example is hemispatial neglect, a condition following a lateralized brain damage characterized, among other things, by an attentional shifting towards the ipsilesional hemispace (Heilman et al., 2003; Kerkhoff, 2001). Patients with hemispatial neglect following right brain damage, when asked to indicate a perceived real centre of a line in a task named Line Bisection Task (LBT), perform a bisection towards the right side of the real centre of a line (Halligan & Marshall, 1988). Similarly, studies on healthy participants describe a leftward bias when participants are asked to perform the LBT (Nicholls, Bradshaw, & Mattingley, 1999). This phenomenon, called pseudoneglect, was firstly described by Browers and Heilman in 1980 and consists in an overestimation of features in the left side of the space (Bowers & Heilman, 1980). Moreover, there is a lot of evidence about the existence of these attentional/visuospatial asymmetries in the absence of direct visual perception. This is the case, for instance, of representational neglect in which the patient does not consider the left side of a mental representation (Bisiach & Luzzatti, 1978; Salvato, Sedda, & Bottini, 2014). In healthy participants, a similar form of such representational asymmetry is described as representational pseudoneglect (McGeorge, Beschin, Colnaghi, Rusconi, & Della Sala, 2007).

Several theories have been developed to explain the above-mentioned attentional asymmetries. For instance, Kinsbourne assumes the presence of two attentional vectors with the left hemispheric vector stronger than the right one (Kinsbourne, 1970). Corbetta et al. propose that a dominance for the right hemisphere that guides attention towards both hemispaces, while the left one only towards the right hemispace (Corbetta et al., 1993). All these models explain well left-hemispatial neglect but are not exhaustive for pseudoneglect as they postulate, in different ways, an advantage for the right hemispace. Siman-Tov et al. (Siman-Tov et al., 2007) have proposed a revised theory. These authors show that both hemifields activate both hemispheres with a low magnitude in the left hemisphere activation compared with the right one. They conclude that there are both a right hemisphere dominance and a left visual field advantage for visual-spatial tasks. In this way, they explaining not only hemispatial neglect but also pseudoneglect in healthy participants.

However, these theories refer to right-handers brain organization and do not take into account brain organization in left-handers. Some studies, focusing on pseudoneglect in the LBT, report stronger biases towards the left side in left-handers compared to right-handers (Luh, 1995; Scarisbrick, Tweedy, & Kuslansky, 1987). Furthermore, there is evidence that which hand is used to perform the task influences the bias magnitude, largely in left-handers than in right-handers (Bradshaw, Nettleton, Wilson, & Bradshaw, 1987; Scarisbrick et al., 1987). Brodie & Dunn (2005) hypothesized that these effects are explained by a right hemisphere dominance for the visuo-spatial tasks in right-handers and a more bilateral/symmetrical activation for the same tasks in left-handers (Brodie & Dunn, 2005). However, it is not clear if this explanation works also for the representational domain.

Many tasks have been used to assess representational pseudoneglect, like the description of a mentally represented familiar scene (McGeorge et al., 2007), tactile rod bisections without visual information (Bowers & Heilman, 1980) or the Mental Number Line Task (MNLT) (Longo & Lourenco, 2007). The latter is widely use because the Mental Number Line (MNL) follows a spatial representation with smaller numbers represented on the left hemispace and higher numbers represented on the right hemispace (Dehaene, Bossini, & Giraux, 1993). The MNLT consists in indicating which number is the half of two given numbers, without making calculations. Usually both patients with neglect and healthy participants manifest a bias in the same direction of the bias manifested in LBT (Loftus, Nicholls, Mattingley, Chapman, & Bradshaw, 2009; Longo & Lourenco, 2007; Zorzi, Priftis, Meneghello, Marenzi, & Umiltà, 2006; Zorzi, Priftis, & Umiltà, 2002). Despite dissociations described in literature between the MNLT and the LBT in both neglect patients and healthy participants (Doricchi, Guariglia, Gasparini, & Tomaiuolo, 2005; Rotondaro, Merola, Aiello, Pinto, & Doricchi, 2015), some studies report strictly related similarities between the LBT and the MNLT (Göbel, Calabria, Farnè, & Rossetti, 2006; Longo & Lourenco, 2007; Zorzi et al., 2006).

2. Aim

The aim of this study was to explore in left-handers and right-handers if visuo-spatial representational processes are affected by the same asymmetries involved in the perceptual ones. If hand dominance, or in other words brain organization, does affect perceptual and representational domains, one would expect a difference between left and right-handers in both domains. Alternatively, if the domains are part of a different sovra-structure, a difference between groups could emerge in one domain but not the other. On the other hand, if brain organization does not affect perceptual and representational domains, no differences should be found between groups.

3. Methods

3.1Participants

The study enrolled 36 participants (mean age: 23.94, SD: ± 4.71; mean education in years: 15.36, SD: ± 1.85) from the student pool of Heriot-Watt University (Edinburgh) in exchange for course credits. Participants were 18 (10 female) right-handers (average laterality quotient: 93.05/100; range: from 75 to 100) and 18 (10 female) left-handers (average laterality quotient: -87.5/100; range: from -100 to -62.5), accordingly to the Edinburgh Handedness Inventory Short Version score (Veale, 2014). Participants were excluded if they declared sensory, neurological or psychiatric impairments, and all of them had normal or corrected to normal vision. All participants were European with the same reading habits from left to right.

Informed consent was obtained prior participation in the experiment. The study was designed according to ethical standards of the Declaration of Helsinki and received approval from the local ethical committee (Approval number: 2016-232).

3.2. Tasks

3.2.1 Laterality Quotient

The Edinburgh Handedness Inventory Short Version (Veale, 2014) was adopted in order to create two different groups (right- and left-handers). The Laterality Quotient (LQ) was calculated as the sum of the items scores divided for the total items number. A score from 100 to 61 was used to enrol right-handers and a score from -61 to -100 was used to enrol left-handers (Veale, 2014).

3.2.2 Line Bisection Task

The Line Bisection Task (LBT) requires to indicate the perceived real centre of different lines. The stimuli were printed lines of four different lengths (120; 140; 160 and 180 mm) measuring 1 mm in width on A4 sheets, in a landscape orientation (Brodie & Dunn, 2005; Brooks, Darling, Malvaso, & Della Sala, 2016). Each sheet presented one line in order to avoid any influence of the previous response on the next one. Each length was repeated 10 times in randomized order. The task was composed by 40 trials divided into two different blocks: in one block, participants signed the perceived real centre with the right hand and in the other block with the left hand. Blocks order was counterbalanced between subjects.

Participants were presented with a sheet with a line in front of them, centred with their subjective body midline. Participants had to mark with a pen the perceived centre of the presented line as fast and as accurately as possible. Then, the next sheet with a line was presented.

As in previous studies (Brooks et al., 2016; Failla, Sheppard, & Bradshaw, 2003; Rotondaro et al., 2015), for each length we collected the individual average bisection error in millimetres, and then transformed it into a percentage. The percentage of deviation was useful in order to compare the LBT bias with the MNLT bias.

3.2.3 Mental Number Line Task

The Mental Number Line Task (MNLT) requires to indicate which number is the half of a given pair of numbers, without making any calculation.

Our task is a modified version of the Longo & Lourenco task (Longo & Lourenco, 2007). The number pairs were non-multiplicative pairs with the smaller number always appearing on the left and the larger one on the right of a fixation cross. The reverse, with the smaller numbers appearing on the right and the larger ones appearing on the left, was not used to avoid a right to left orientation of the MNL. We chose non-multiplicative pairs because multiplication knowledge can influence the performance (Nuerk, Geppert, van Herten, & Willmes, 2002). The smaller numbers ranged from 10 to 80 and the larger ones from 22 to 98, avoiding intervals not divisible by 2 (Longo & Lourenco, 2007). The difference between the numbers in each pair was 12, 14, 16 or 18 units in order to match the lines lengths and to avoid possible ceiling effects with difference value lesser or equal to 10 (Longo & Lourenco, 2007). Each range was repeated 10 times in a randomized order. There were 40 trials in total, divided in two blocks. Blocks order was counterbalanced between participants. All the stimuli were presented on a pc screen (13.3’’; 16:9) with a resolution of 1920 x 1080, using Psycho-Py 1.83.03 (Psychology software in Pyton) (Peirce, 2007).

Participants seated in front of the pc screen at the distance of 50 cm with their right or left index fingers, depending on the block order, on the space bar. After the instructions, a pair of numbers appeared on the screen preceded by a fixation cross lasting 1000 ms. Participants had to say aloud the half number of the pair and press the space bar to continue to the next pair of numbers. They had to be as quick and as accurate as possible. They were instructed to do not make calculation to solve the task and practice trials were shown prior to the real task. Participants' verbal responses were collected by the experimenter.

3.3 Data analysis

Data were analysed with Statistical Package for Social Science (IBM® SPSS® Statistic, Version 20).

For each task and for each participant we collected bisection error measurements. For the LBT, the error was computed as the bisection mark distance from the left endpoint of the line – real centre measurement from the left endpoint of the line (Failla et al., 2003). For the MNLT, the bisection error was computed as the participant response – half number of the pair (Göbel et al., 2006). In both tasks, a positive value represented a rightward bias and a negative value represented a leftward bias. In both the LBT and the MNLT, we considered the mean bisection error for each length and for each hand separately, and we converted the error measurement into a percentage of stimulus length, accordingly to the standard method to compute bisection performance (Brooks et al., 2016). The percentage expressing the error measurement in each task for both the right and the left hand, averaging all the lengths, was the dependent variable considered during the statistical analysis.

Firstly, we checked for the bias difference from zero by means of one-sample t-tests in each group and in each task separately. Then, we performed a repeated measures ANOVA with Task (LBT, MNLT) and Hand (right, left) as within subjects factors and Group (right-handers, left-handers) as between subjects factor. We followed these passages to firstly check if the bias was manifested in both tasks by both groups and, secondly, to explore groups and tasks differences on the bias magnitude.

Lastly, we performed a correlation analysis using Pearson coefficient between the bias in MNLT and the bias in LBT for each group and each hand separately. This analysis allowed to explore the relation between perceptual and representational domain.

Alpha level was set at $p <.05$, post hoc comparisons were performed by means of estimates marginal means Bonferroni corrected for multiple comparisons. We report the effect size for significances as partial η^2 (η^2_p) values.

4. Results

4.1 Bias difference from zero

The overall bias, in the right-handers group, was significantly different from zero in both the LBT ($t_{(17)} = -3.119$; $p = .006$) and the MNLT ($t_{(17)} = -5.577$; $p < .001$). In the left-handers group, the overall bias was significantly different from zero in the MNLT ($t_{(17)} = -5.215$; $p <.001$) but not in the LBT ($t_{(17)} = -2.010$; $p = .061$).

Because the hand used to perform bisection tasks modulates the performance more in left- than right-handers (Bradshaw et al., 1987; Scarisbrick et al., 1987), it is worth considering the bias difference from zero as a function of the hand used. This ensures to explore the phenomenon taking into consideration the confounding role played by the hand in the above mentioned results. In the left-handers group, the bias was different from zero in the LBT when the task was performed with the left hand ($t_{(17)} = -3.417$; $p = .003$) but not with the right hand ($t_{(17)} = .901$; $p = .380$). In the MNLT, instead, the bias was different from zero when the task was performed with both the left ($t_{(17)} = -5.124$; $p < .001$) and the right hand ($t_{(17)} = -3.681$; $p = .002$) (figure 1 - a). In the right-handers group, the bias was different from zero in the LBT performed with the left hand ($t_{(17)} = -3.413$; $p = .003$) and there was a trend when the task was performed with the right hand ($t_{(17)} = -2.111$; $p = .05$). The bias was different from zero also in the MNLT with both the right ($t_{(17)} = -2.832$; $p = .011$) and left ($t_{(17)} = -6.122$; $p < .001$) hand (figure 1 - b).

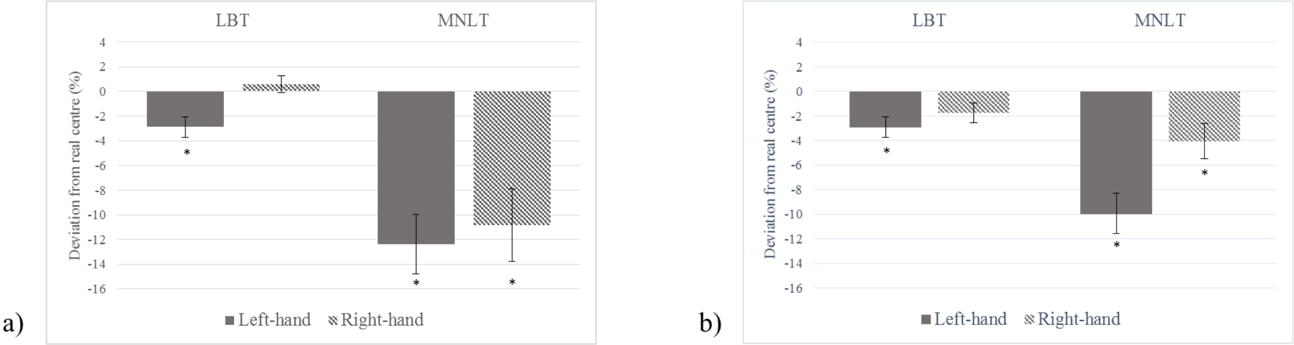


Figure 1. *Bias difference from zero in the left-handers group (a) and in the right-handers group (b) expressed in percentage for both the right and the left hand in the Line Bisection Task (LBT) and the Mental Number Line Task (MNLT). Numbers on the y-axis refer to bias in percentage (negative numbers indicate a bias towards the left hemispace). Textured bars represent the bias when the right hand was used; solid bars represent the bias when the left hand was used. Stars represent a significant difference. Bars indicate the standard error of the mean*.

In summary, a leftward bias was present in the MNLT for both the right- and the left-handers group with both hands. Conversely, both right- and left-handers showed a leftward bias only with the left hand in the LBT. The two groups seemed to show the same pattern of performance when hand is taken into account, although differences are apparent if the performance is considered across tasks regardless the hand used. Because any further differences could be related to the different bias magnitude in the two groups, we performed a repeated measures ANOVA predicting to find an interaction between Group and Task if the bias magnitude is differently modulated by the specific domain (representational, perceptual). In other words, this prediction is supported by the results in the previous analysis in which a difference between groups' performance is apparent only without considering the role of the hand used. The results are reported in the following section.

4.2 Main analysis

We found a significant main effect of Task [$F_{(1, 34)} = 30.575$; $p < .001$; $\eta^2_p = .473$], driven by a bias farther to the left in the MNLT (Mean= -9.307; SE= 1.278) compared to LBT (Mean= -1.727; SE= .467). Secondly, we found a main effect of Hand [$F_{(1, 34)} = 12.740$; $p = .001$; $\eta^2_p = .273$] driven by a bias farther to the left when the task was performed with the left hand (Mean = -7.026; SE = .753) compared to the right hand (Mean = -4.007; SE = .838). No main effect of Group was found [$F_{(1, 34)} = 1.624$; $p = .211$; $\eta^2_p =.046$].

Secondly, we found a significant interaction between Task and Group [$F_{(1, 34)} = 4.476$; $p = .042$; $\eta^2_p =.116$]. There was a significant difference between the MNLT and the LBT in both right-handers (Mean difference = 4.680; SE = 1.939; p = .021) and left-handers (Mean difference = 10.480; SE = 1.939; p < .001) and this difference was greater in left- than right-handers ($t_{(34)} = 2.116$; $p = .042$). Specifically, the bias was farther to the left in the MNLT (right-handers: mean = -6.996; SD = 1.808; left-handers: mean = -11.618; SD = 1.808) than in the LBT (right-handers: mean = -2.316; SD = .660; left-handers: mean = -1.137; SD = .660) (figure 2).

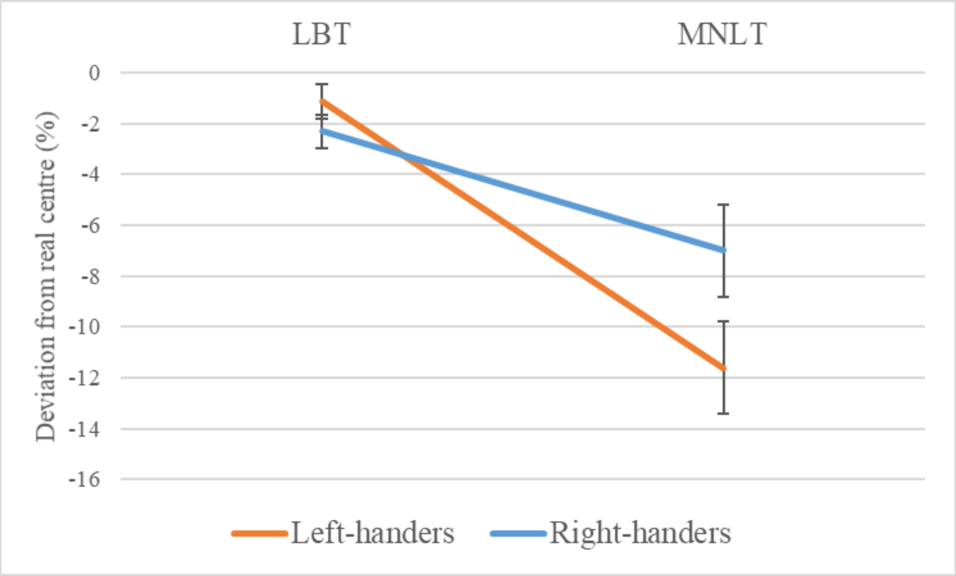


Figure 2. *Interaction between tasks (Line Bisection Task – LBT and Mental Number Line Task – MNLT) and groups (right- and left-handers). Orange line represents left-handers, blue line represents right-handers. Numbers on y-axis refer to bias expressed in percentage. Negative numbers represent a bias toward the left hemispace. Bars represent the standard error of the mean.*

No significant interactions were found neither between Hand and Group [$F_{(1, 34)} = .361$; $p = .552$; $\eta^2_p = .010$], nor between Hand and Task [$F_{(1, 34)} = .456$; $p = .504$; $\eta^2_p = .013$], nor between Hand, Task and Group [$F_{(1, 34)} = 2.689$; $p = .110$; $\eta^2_p = .073$].

4.3 Correlation between Mental Number Line and Line Bisection task

In right-handers group no correlation was found between bias in MNLT and bias in LBT neither with the right ($r = -.216$; $p = .389$) nor with the left hand ($r = .143$; $p = .570$).

In left-handers group, no correlation was found between bias in MNLT and bias in LBT neither with the right ($r = -.029$; $p = .909$) nor with the left hand ($r = -.301$; $p = .225$).

5. Discussion

Differences have been reported between right- and left-handers in the perceptual domain (Bradshaw et al., 1987; Brodie & Dunn, 2005; Luh, 1995; Scarisbrick et al., 1987). However, no studies explored yet differences between right- and left-handers in the representational domain. To this aim, we investigated if the representational domain is affected by the same asymmetries involved in the perceptual one in both right- and left-handers. This comparison allows an indirect inference on how the space is represented and attended in differently lateralized individuals. In this study, 18 right-handers and 18 left-handers carried out two different tasks: the LBT to explore the perceptual domain and the MNLT to explore the representational one. Both tasks were performed with the right and the left hand as the hand used to perform the task can modulate the performance (for a review see Jewell & McCourt, 2000).

Our results suggested that attentional asymmetries affect the perceptual and representational domain in the same direction in both right- and left-handers. Specifically, the bias was farther to the left in the representational domain than in perceptual one in both groups. However, the two groups differed in the bias magnitude regarding the specific domain. Indeed, the difference between the bias in the representational domain and that in the perceptual one was greater in left- than right-handers. This difference seems to be led by a greater leftward bias for left- than right-handers in the representational domain.

In order to explain our results, hemispheric visuo-spatial attention lateralization can be taken into account. Several studies postulate that visuo-spatial attention is mainly lateralized to the right (Cai, Van Der Haegen, & Brysbaert, 2012; Fink, Marshall, Weiss, & Zilles, 2001; Foxe, McCourt, & Javitt, 2003). This fact must be considered besides cognitive theories explaining the bias as the result of an imbalance between the right and the left hemispheres (Corbetta et al., 1993; Kinsbourne, 1970; Siman-Tov et al., 2007). Specifically, in right-handers, an imbalanced activation of hemispheres is postulated with the right hemisphere being the main agent in visuo-spatial processes (Bradshaw,

Bradshaw, Nathan, Nettleton, & Wilson, 1986). Differently, left-handers are less lateralized in terms of a more symmetrical activation during tasks than right-handers (Brodie & Dunn, 2005). This could in principle explain why left-handers did not manifest any bias in the perceptual domain when the performance has been considered regardless the hand used.

Considering the role of the hand in the perceptual domain, a similar explanation can be applied. Instead of considering only the magnitude of "spatial attraction" led by the "main hemisphere", the left bias can easily be seen as an increase of noise (due to the overlap or simultaneous processing of motor and perceptual information) for the right hemisphere, with a resulting variable shifting towards the left side of space. Consequently, introducing noise (i.e. motor information for the left hand) in this system could provoke a greater bias. Indeed, both right- and left-handers manifested clearly the bias with the left but not with the right hand in the perceptual task (LBT). However, right-handers manifested a trend towards the left side with the right hand. Theoretically, when noise is introduced in the hemisphere which is active at a hypothetic 60% (the right hemisphere), left-handers show a leftward bias because the critical threshold is surpassed. Differently, if noise is introduced in the hemisphere which is active but not drastically reduced (hypothetical 40%, the left hemisphere), the bias does not appear because the threshold is not surpassed. Similarly, in right-handers when noise is introduced in the hemisphere activated at a hypothetic 70% (right hemisphere) a leftward bias emerges as well. Introducing noise in the hemisphere activated at a hypothetic 30% (left hemisphere) in right-handers, the bias does not appear and the right hemisphere seems still to maintain its predominance, resulting in a trend towards the left side of space with the right hand. Our results challenge those found by Brodie and Dunn (Brodie & Dunn, 2005). These authors suggest an absence of hemispheric dominance for visuo-spatial tasks in left-handers and assume that a unimanual response during a LBT activates both hemispheres equally. They find a reversed pseudoneglect (the bias is towards right) in left-handers when they use the dominant hand. According to this study, the bias in the LBT is due to an interaction between different factors (cerebral activation related to manual response, hemispheric asymmetries and scan direction) (Brodie & Dunn, 2005). However, this theory cannot account for the absence of bias when the right-hand is used.

The same explanation might not to be appropriate in the representational domain, as we found a clear bias towards the left side with both hands in both groups. This result highlights the pivotal role played by motor demands in influencing the bias magnitude. The LBT is a visuo-motor task and the use of the right instead of the left hand could work as a cue directing the attention more on the right or on the left side of the space respectively (Halligan, Manning, & Marshall, 1991). The same is not true in the MNLT in which the motor act is not an intrinsic feature of the task. In our task, the response was given verbally and the motor act required by the task was useful only in order to pass to the next trial. In keeping with that, this level of motor involvement would be not enough to affect the leading right hemisphere. In particular, the MNL is related to the activity of the superior posterior parietal lobe in the right hemisphere (Dehaene et al., 2003) so that a durable bias towards the left side of the representational space might be hypothesized. Furthermore, the greater difference found in left-handers between the bias in the perceptual than in the representational domain might be related to a greater noise provoked by the verbal demands in the MNLT compared to motor requirements in LBT. This last point is supported by evidence of the higher probability of right-lateralized language functions in left- than in right-handers (Knecht et al., 2000; Pujol, Deus, Losilla, & Capdevila, 1999). As attested in literature, the involvement of the same hemisphere in both language and spatial processes affects the latters (Lansdell, 1969; Teuber, 1974) and so, the greater interference corresponds to a greater leftward bias. However, this hypothesis remains a mere speculation and more studies are needed in order to clarify those factors that intervene and interfere with attentional processes in the MNLT.

Lastly, it must be considered that the two tasks are different because the bias had a greater magnitude in the representational domain (MNLT) compared to the perceptual one (LBT). The same difference was described by other studies (Brooks et al., 2016; Longo & Lourenco, 2007) and suggests that the

MNLT is more sensitive to detect pseudoneglect than the LBT (Göbel et al., 2006). At this point, one could hypothesize that the two tasks are not controlled by the same attentional mechanisms, as we found an absence of correlation between them. In a study of Rotondaro et al. (2015), the authors draw the same conclusions and stated that physical lines and the mental number line are inspected in a different way (Rotondaro et al., 2015). However, the authors used a verbal version of the MNLT to avoid any cue for a left-to-right organisation of the Number Line. We used visual stimuli with the smaller number appearing always on the left because we wanted to maintain the same left-to right inspection assumed in the LBT. In any case, independently from the reason behind the differences between representation and perception, left-handers and right-handers manifest differences depending on tasks, suggesting that at the hierarchical level, higher sovra-structures are different between these populations. In other words, if the general process is considered (i.e. how the attentional asymmetries affects different domains), differences are apparent suggesting that different factors intervene in right- and left-handers regarding the task used.

Chapter 3

The contribution of right and left parietal cortex in bimanual temporal coupling

1.Introduction

The hands are a fundamental mean to interact with the environment. During the human evolution, our species developed many manual abilities to perform complex actions, handle objects and perform gestures. All of these abilities are accompanied by the development of motor coordination: we can move our hands synchronously at the same time or asynchronously, moving the right and left hand in different moments (Swinnen, 2002). Furthermore, it is possible to distinguish congruent movements, when the two hands perform the same movement, or incongruent movements, when the two hands perform at the same time different movements (Swinnen, 2002). Taking into consideration the bimanual coordination, mainly two theories tried to explain this phenomenon. The first one stated that a unique motor program exists for both the hands because the entire motor command is decided (Kelso, Southard, & Goodman, 1979b; Schmidt, 1975). The second theory, based on the inter-manual cross-talk, stated that two different motor programs exist for right and left hand respectively (Marteniuk & MacKenzie, 1980; Marteniuk, MacKenzie, & Baba, 1984). The first theory seems to better account for the behavioural evidence of an interference between two limbs when they perform different movements at the same time (Bozzacchi, Cimmino, & Di Russo, 2017). This phenomenon is known as bimanual coupling effect (Walter, Swinnen, Dounskaia, & Van Langendonk, 2001) and it has been described in two different domains: spatial and temporal.

The bimanual spatial coupling effect is usually explored by means of the circle-line paradigm (Franz, Zelaznik, & McCabe, 1991). In this task, participants are required to draw lines with one hand and circles with the other hand. As the result, the shape of each drawing tends to become oval: the lines tend to become circles and *vice versa* (Franz et al., 1991). The bimanual temporal coupling effect has been studied using reaching task in which participants are required to perform movements towards targets in different positions with the two hands at the same time (Kelso, Southard, & Goodman, 1979a, 1979b). The seminal works of Kelso et al. (Kelso et al., 1979a, 1979b) in this field are based on a mathematical law, namely the Fitts' law (Fitts & Peterson ', 1964). The Fitt's law describes the Movement Time (MT) change regarding the dimension and the position of different targets. Accordingly, the MT is expressed by the following mathematical formula: MT = $a+blog2\ (2A/W)$ in which MT depends on the ratio between movement amplitude (A) and target dimension (W), given some constants (a and b) (Fitts & Peterson ', 1964). For instance, the time needed to perform a movement toward a 0.5 cm target with a distance of 4 cm, would be the same compared to a movement toward a 1 cm target with a distance of 8 cm. Kelso et al. falsified the Fitts' law in case of bimanual incongruent movements (Kelso et al., 1979a). In their study, participants were required to reach different targets with one or two hands simultaneously. The targets could be different in size (small or large) and in position (near or far). The authors noticed that, in case of bimanual incongruent movements (e.g one hand reaches the large-near target while the other hand reaches the small-far target), the two hands started and finished the movements at the same time, even if they performed actions towards different sized targets located at different distance (Kelso et al., 1979a). From this first study, the same paradigm and its modified versions have been extensively used (Bozzacchi et al., 2017; Buckingham, Main, & Carey, 2011; Riek, Tresilian, Mon-Williams, Coppard, & Carson, 2003; Shea, Boyle, & Kovacs, 2012; Weigelt, 2007) and they have been also applied to the study of patients with motor impairments after stroke (Pia et al., 2013; Rose & Winstein, 2013). Therefore, the use of this paradigm makes it a feasible tool to study the bimanual temporal coupling.

As for neural underpinning of the bimanual coupling, the Supplementar Motor Area (SMA) has been described as the main agent for the bimanual coordination (Sadato, Yonekura, Waki, Yamada, & Ishii, 1997). The first studies on monkey's brain ablation showed how, without SMA, there were permanent bimanual coordination impairments (Brinkman, 1981). To date, it is well known its role for motor act selection (Deiber et al., 1991), motor learning (Roland, Eriksson, Widen, & Stone-Elander, 1989), motor planning (Orgogozo & Larsen, 1979) and motor programming (Roland, Larsen, Lassen, & Skinhøj, 1980) but other brain areas are part of the more extensive network withstanding the bimanual coordination (Sadato et al., 1997). For instance, a role of the cerebellum, the Premotor Cortex (PMC) and the cingulated Motor Area (CMA) has been described as well (Immisch, Waldvogel, van Gelderen, & Hallett, 2001; Sadato et al., 1997; van den Berg, Swinnen, & Wenderoth, 2010). In particular, another area attracting the attention of the researchers is represented by the parietal area as it has a role in integrating sensory information into a spatial reference frame for motor planning (Cohen & Andersen, 2002). The involvement of the parietal areas is described when interference arise during bimanual coordination tasks and during bimanual incongruent finger tapping (Ullén, Forssberg, & Ehrsson, 2003; Wenderoth, Debaere, Sunaert, & Swinnen, 2005). Furthermore, the involvement of the parietal areas has been described during the circle-line drawing paradigm evaluating the spatial coupling effect (Garbarini et al., 2014). In detail, the authors found an activation of the Posterior Parietal Cortex (PPC) specific for incongruent bimanual movements and the result is interpreted in light of the spatial connotation of the task and the role played by the PPC in the production of complex actions due to the spatial integration processes (Garbarini et al., 2014). Another study, evaluating the bimanual temporal coupling effect, found an activation of the Superior Parietal Lobule (SPL) specific for incongruent bimanual movements (Diedrichsen, Grafton, Albert, Hazeltine, & Ivry, 2005). In this study, participants were required to perform reaching movements towards targets located forward or sideward. The incongruent movements required to perform a forward movement with one hand and a sideward movement with the other hand. The authors stated that, in this condition, a more complex spatial representation is required to perform different movements regarding different location. Differently, during congruent movements the reaching movements can be performed demanding attention only to one target (Diedrichsen et al., 2005). The SPL would represent a locus of movement-related interference (Diedrichsen et al., 2005).

As for the lateralization of the bimanual coupling effect, evidence support a dominance for the right hemisphere (Diedrichsen et al., 2005; Garbarini et al., 2014; van den Berg et al., 2010; Wenderoth, Debaere, Sunaert, Hecke, & Swinnen, 2004). For instance, Wenderoth et al. (2004) stated that the bimanual interference is mainly related to the activation of superior parietal, intraparietal and dorsal premotor areas in the right hemisphere (Wenderoth et al., 2004). Similarly, van den Berg et al. (2010) assumed a functional asymmetry of the PMC leaded by the bimanual or unimanual nature of the task: a right lateralization of this area would be related to bimanual tasks (van den Berg et al., 2010). However, other studies show a dominance of left hemisphere in different kind of bimanual movements (Stucchi & Viviani, 1993; Walsh, Small, Chen, & Solodkin, 2008).

2. Aim

The aim of the present study was to explore the lateralization of the bimanual temporal coupling effect focusing on the parietal area. For this reason, we applied the tDCS (sham, anodic and cathodic) over both the right and left parietal areas (P4 and P3). If the right hemisphere has a pivotal role in the bimanual temporal coupling effect during visuo-spatial tasks, we hypothesized to find a modulation of the effect during tDCS stimulation over the right than the left parietal area. Specifically, it is predicted the disruption of the temporal coupling effect when the cathodic (inhibitory) modulation is applied over the right parietal area.

3. Methods

3.1 Participants

Thirty-two healthy participants (22 F; mean age ± standard deviation: 22.93 ± 3.78; mean education ± standard deviation: 15.93 ± 1.47) were recruited from the student pool of the University of Pavia in exchange of course credits. All participants were right handed as measured by the Edinburgh Handedness Inventory (Oldfield, 1971), reported absence of previous history of mental or neurological diseases, absence of drug treatment and had normal or corrected to normal vision.

Inclusion criteria for the administration of the tDCS were: absence of heart disease, absence of history of epilepsy until grandparents, absence of metallic objects in the body, absence of history of migraine with aura phase and, for the women, absence of pregnancy.

Informed consent was obtained prior participation in the experiment. The study was designed according to ethical standards of the Declaration of Helsinki and received approval from local University of Pavia' committee.

3.2 tDCS procedure

tDCS stimulation was delivered by a battery-driven constant current stimulator (BrainSTIM E.M.S. s.r.l.) using a pair of surface saline soaked sponge electrodes (5cm x 5cm) placed on the target areas of stimulation. Conductive gel was put under the sponges to facilitate electric conductance. Stimulation intensity was set at 2 mA for 20 minutes with a ramp up and a ramp down periods of 30 seconds at the start and at the end of stimulation, complying with current safety guidelines (Nitsche et al., 2008).

Extracephalic montage was used: the active electrode was placed over the target area and the reference electrode was placed on the right deltoid because extracephalic montage allow us to make more robust predictions about cortical modulation independently of reference electrode location (Im, Park, Shim, Chang, & Kim, 2012). Areas of interest were identified using the international 10-20 system for EEG electrode placement (Jasper, 1958).

All participants completed three tDCS conditions with different types of stimulations (Sham, Anodic and Cathodic) over two different experimental sessions, separated by 1 week to avoid interference effects between the different stimulation types. We used a group design experiment: each participant received tDCS stimulations over only one area of interest.

Anodic stimulation consists in applying electric current over the target area to depolarize the cellular membrane and so to excite the cortical target area. Cathodic stimulation consists in applying electric current over the target area in order to iper-polarize the cellular membrane and so to inhibit the cortical target area. During the sham stimulation, there was a ramp up period of 30 seconds followed by a ramp down period of 30 seconds. This ensured that the participants felt the initial itching sensation as if it were a true stimulation. Participants were always naive about the type of stimulation. tDCS conditions' order was counterbalanced and randomized between subjects.

In the first session, the active stimulation was always preceded by the Sham stimulation to record a baseline performance.

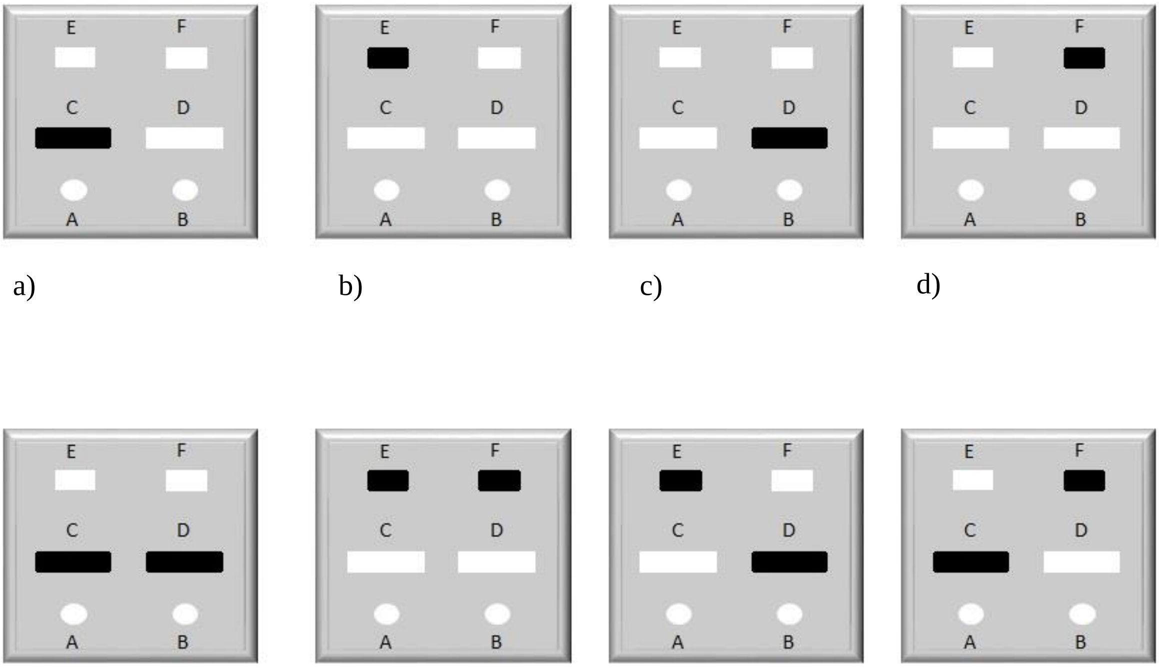
Participants were randomly assigned to one of the two groups on the basis of the area to stimulate (P4, P3).

3.3 Task

We used a modified version of the Kelso et al.' paradigm (Kelso et al., 1979a) to explore how right and left hands coordinate each other in different way on the basis of the movement type.

The experimental apparatus consisted in a rectangular plexiglass board (31,2 cm long, 31 cm wide, 4 cm thick) with six keys, three on the right and three on the left of the participants' body midline: two circular home keys (diameter: 2cm) placed 5 cm from the right and left edge respectively and placed 2 cm from the low edge; two rectangular large keys (7cm x 2cm) placed 5cm above the right and left home keys respectively and two rectangular small keys (3,8cm x 2cm) placed 21 cm above the right and the left home keys respectively. The task consisted in reaching the target keys (small, large or both) starting from the home keys (the detailed task procedure is explained below).

There were eight possible combinations in total (figure 1): (i) Unimanual Near Right; (ii) Unimanual Near Left; (iii) Unimanual Far Right; (iv) Unimanual Far Left; (v) Bimanual Congruent Near; (vi) Bimanual Congruent Far; (vii) Bimanual Incongruent Near Right-Far Left; (viii) Bimanual Incongruent Near Left-Far Right.



a) b) c) d)

e) f) g) h)

Figure 1. *The eight possible combinations of movements are depicted in the figure. In the upper part of the picture: unimanual movements for both left (a and b) and right (c and d) hands. In the lower part of the picture: bimanual congruent (e and f) and incongruent (g and h) movements. A and B refer to the home keys. C and D indicate the near-large target keys. E and F indicate the far-small target keys. See the main text for the detailed description of each movement condition represented in the picture.*

In the Unimanual (U) conditions participants had to reach one target key (left or right) with their respective index finger (left or right) while the other index finger remained on the home key. In the Bimanual Congruent (BC) conditions participants had to reach two target keys either near or far with both left and right index fingers. In the Bimanual Incongruent (BI) conditions participants had to reach the near target key with right index finger and the far target key with left index fingers or *vice versa* (see figure 1). The task was composed by 120 trials, 15 for each of the eight possible combinations.

At the beginning of each trials the participants placed their right and left index fingers on the right and left home keys respectively. The task required to move the right and left index fingers as fast and as accurately as possible from the home keys to the specific target keys and then to return to the home keys. The target keys were specified each time by indicator light which switched off as soon as the participant reached the keys. The target keys could light up in three different conditions (Unimanual, Bimanual Congruent, Bimanual Incongruent) and in two different position (Near, Far). The indicator light remained on until participants gave the response. Between each trial, participants were instructed to look at a led, place on the top of the board, which switched on before the starting of each trial. Differently from Kelso et al. (1979a), we used a visuo-spatial cue as warning stimulus prior to perform the movement in order to control the visuo-spatial attention before to start each movement, in other words, the led served as a fixation point.

The board was connected to a computer in order to collect both Reaction Times (RTs - calculated as the time from target keys lighting to the fingers leaving from the home key) and Movement Times (MTs - calculated as the time from the fingers leaving from the home keys to the fingers contact with the target keys).

3.4 Data analysis

Data were analysed with Statistical Package for Social Science (IBM® SPSS® Statistic, Version 20).

Reaction Times (RTs) and Movement Times (MTs) have been pre-processed for outliers using a cut-off of two standard deviations above and below the participants' mean. Values below the mean have been considered indicative of anticipations while values above the mean have been considered indicative of lack of attention during task execution (Ratcliff & Roger, 1993).

After data pre-processing, we obtained means for each one of eight possible combinations for each participant. Then we divided the participants' means based on the group belong to (P4 and P3).

Right and left hand have been analysed separately due to the different velocity between hands (Buckingham, Binsted, & Carey, 2010; Buckingham et al., 2011; Buckingham & Carey, 2009; Shen & Franz, 2005). Because in this way a direct comparison between the two hands it would not possible, the Inter Response Interval (IRI) has been calculated in accordance with another study using a similar bimanual temporal coupling paradigm (Weigelt, 2007). It was calculated as an absolute value subtracting the left hand's RTs and MTs from the right hand's RTs and MTs respectively (Weigelt, 2007). In this way, an index related to the temporal disparity at the start and at the end of each bimanual movement (Congruent and Incongruent) was created.

For both RTs and MTs, we applied a repeated measures ANOVA with tDCS (Sham, Anodic and Cathodic), Condition (U, BC and BI) and Position (Near and Far) as within subjects factors and Group (P4 and P3) as between subjects factor.

For IRIs, it was firstly checked their difference from zero by mean of one-sample t-test. Then, we applied a repeated measures ANOVA with tDCS (Sham, Anodic and Cathodic), Condition (BI and BC) and Location (Start and End) as within subjects factors and Group (P4 and P3) as between subjects factor.

Alpha level was set at $p = .05$ for all analyses. Post-hoc comparisons have been performed by means of estimated marginal means Bonferroni corrected. We report the effect size for significances as partial eta squared (η_p^2) values.

The interaction between Condition and Position on MTs was considered indicative of the bimanual temporal coupling effect (where difference between Near and Far positions decreases in the BI condition because of bimanual coordination). Because the primary aim of the present study was to evaluate the parietal lobe contribution to the bimanual temporal coupling effect, it was predicted to find a three-way interaction (tDCS*Condition*Position) on MTs and, possibly, different effect of tDCS regarding the stimulated area (P4 or P3). Furthermore, we also explored the general involvement of right and left parietal areas in the bimanual paradigm. For this reason, RTs and IRIs were considered as well.

4. Results

4.1 Reaction Times

Right hand

On the right hand we found a main effect of tDCS [$F_{(2, 60)} = 4.930$; $p =.010$; $\eta_p^2 = .141$]. Specifically, there was a difference between Sham and Anodic stimulation (Mean difference = 17.999; SE = 6.095) driven by faster RTs in Anodic (Mean = 352.480; SE = 7.456) than Sham stimulation (Mean = 370.479; SE = 7.242). Neither main effect of Condition [$F_{(2, 60)} = 1.382$; $p =.259$; $\eta_p^2 = .044$], nor of Position [$F_{(1, 30)} = .029$; $p =.865$; $\eta_p^2 = .001$], nor of Group [$F_{(1, 30)} = .837$; $p =.368$; $\eta_p^2 = .027$] were found.

The interaction between Condition and Position was significant [$F_{(2, 60)} = 10.137$; $p < .001$; $\eta_p^2 = .253$] driven by a difference between near and far position in both U (Mean difference = 11.354; SE = 4.510; $p = .017$) and BI (Mean difference = 10.851; SE = 4.725; $p = .029$) conditions but not in BC condition (Mean difference = 2.355; SE = 4.604; $p = .613$). In U condition RTs in near position (Mean = 351.017; SE = 7.055) resulted faster than RTs in far position (Mean = 362.371; SE = 8.196). Conversely, in BI condition RTs in near position (Mean = 366.812; SE = 6.950) resulted slower than RTs in far position (Mean = 355.961; SE = 8.132) (figure 2).

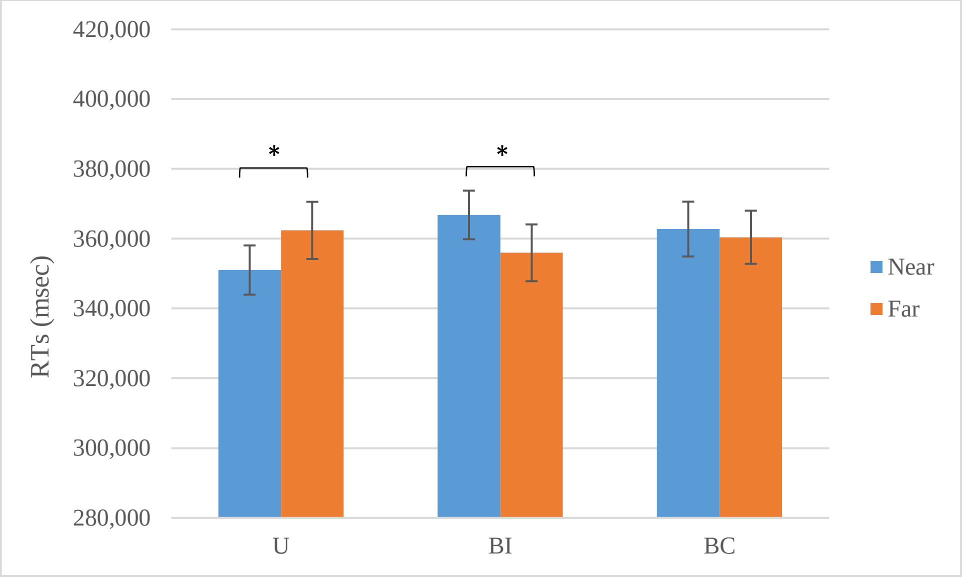


Figure 2. *Interaction between condition and position for the right hand. RTs in milliseconds for Unimanual (U), Bimanual Incongruent (BI) and Bimanual Congruent (BC) conditions are depicted. Blue bars represent the RTs in near position. Orange bars represent the RTs in far position. Black bars represent the standard error of the mean. Stars represent a significant difference.*

Also the interaction between tDCS and Position resulted significant [$F_{(2, 60)} = 3.352$; p =.042; $\eta_p^2 = .100$]. There was a difference between RTs in Sham and RTs in both Anodic (Mean difference = 23.342; SE = 6.023; p = .002) and Cathodic stimulation (Mean difference = 20.827; SE = 6.148; p = .006) only in near position. Specifically, RTs in both Anodic (Mean = 351.577; SE = 6.894) and Cathodic stimulation (Mean = 354.092; SE = 8.362) were faster compared to RTs in Sham stimulation (Mean = 374.919; SE = 7.633). Furthermore, also the interactions between tDCS, Condition and Position [$F_{(4, 120)} = 3.281$; p =.014; $\eta_p^2 = .099$] and between tDCS, Condition, Position and Group [$F_{(4, 120)} = 2.496$; p =.046; $\eta_p^2 = .077$] resulted significant

Because of this last interaction, data were re-analyzed in each group separately for the right hand including tDCS, Condition and Position as within subjects factors.

P4

In P4 we found a main effect of tDCS [$F_{(2, 32)} = 3.860$; $p = .031$; $\eta_p^2 = .194$] led by a trend in the difference between Sham and Cathodic stimulation. Participants showed a trend with faster RTs in Cathodic (Mean = 357.693; SE = 9.746) than Sham stimulation (Mean = 377.753; SE = 8.459), however this difference did not reach any significance (Mean difference = 20.060; SE = 8.165; p = .077). No main effect of Condition [$F_{(2, 32)} = 1.267$; $p = .296$; $\eta_p^2 = .073$] and Position [$F_{(1, 16)} = .100$; $p = .755$; $\eta_p^2 = .006$] were found.

We also found an interaction between Condition and Position [$F_{(2, 32)} = 10.548$; $p < .001$; $\eta_p^2 = .397$]. Specifically, participants showed faster RTs for far (Mean = 360.686; SE = 8.928) than near position (Mean = 373.778; SE = 8.322) in the BI Condition only (Mean difference = 13.092; SE = 5.566; p = .032). Neither interaction between tDCS and Condition [$F_{(2, 32)} = 1.497$; $p = .214$; $\eta_p^2 = .086$] nor between tDCS and Position [$F_{(2, 32)} = 1.473$; $p = .244$; $\eta_p^2 = .084$] nor between tDCS, Condition and Position [$F_{(4, 64)} = 1.180$; $p = .328$; $\eta_p^2 = .069$] were found.

P3

In P3 we only found a three way interaction between tDCS, Condition and Position [$F_{(2, 56)} = 3.519$; $p = .012$; $\eta_p^2 = .201$]. For this reason, three different repeated measures ANOVA were applied for each condition (U, BC, BI) considering tDCS and Position as within subjects factors.

In both U and BI conditions, neither main effects nor interactions were found.

In BC condition there was a main effect of tDCS [$F_{(2, 28)} = 3.680$; $p = .038$; $\eta_p^2 = .208$]. Specifically, there was a trend between faster RTs during anodic stimulation (Mean = 341.256; SE = 8.989) compared to sham stimulation (Mean = 369.097; SE = 10.999) that, however, did not reach any significance (Mean difference = 27.841; SE = 10.713; p = .063). Furthermore, the interaction between tDCS and Position resulted significant [$F_{(2, 28)} = 6.712$; $p = .004$; $\eta_p^2 = .324$]. Specifically, only in near position both Anodic and Cathodic stimulation reduced RTs compared to Sham stimulation (Anodic:

mean difference = 48.700; SE = 14.835; p = .016; Cathodic: mean difference = 47.653; SE = 14.461; p = .016) (Figure 3).

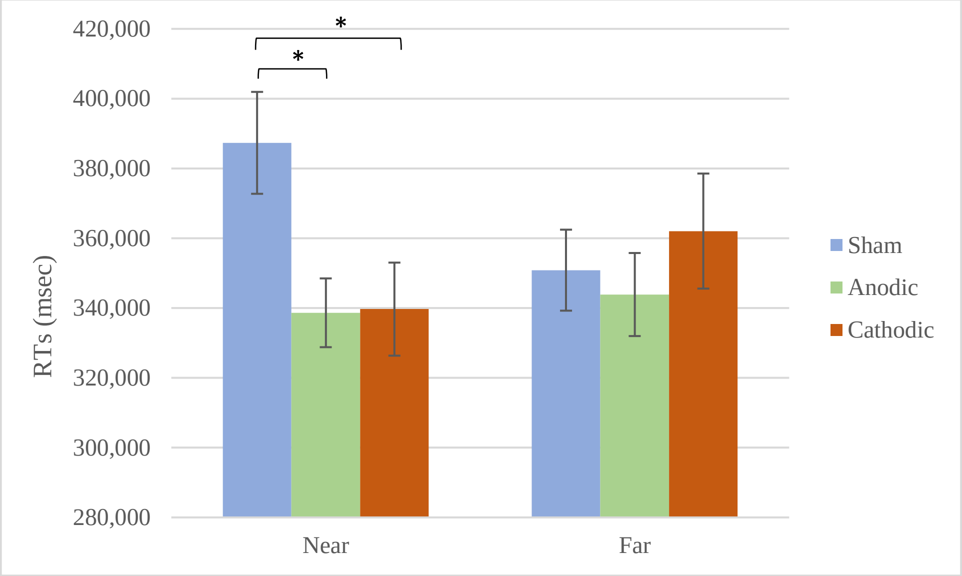


Figure 3. *Interaction between tDCS and Position for the right hand in Bimanual Congruent Condition. RTs in milliseconds are depicted for near and far positions in each kind of stimulation. Blue bars represent Sham stimulation. Green bars represent Anodic stimulation. Red bars represent Cathodic stimulation. Black bars represent the standard error of the mean. Stars indicate a significant difference.*

Left hand

On the left hand we found a main effect of Condition [$F_{(2, 60)} = 9.262$; $p < .001$; $\eta_p^2 = .236$] driven by faster RTs in U (Mean = 338.312; SE = 6.954) than both BC (Mean =351.025; SE = 7.331; p = .002) and BI (Mean = 346.230; SE = 7.548; p = .015) conditions. There was also a main effect of Position [$F_{(1, 30)} = 4.751$; $p = .037$; $\eta_p^2 = .137$] driven by faster RTs in far (Mean = 342.735; SE = 7.148) than near position (Mean = 347.643; SE = 7.180). Neither main effect of Group [$F_{(1, 30)} = 1.194$; $p = .283$; $\eta_p^2 = .038$] nor main effect of tDCS [$F_{(2, 60)} = 2.608$; $p = .082$; $\eta_p^2 = .080$] were found.

We also found a significant interaction between Condition and Position [$F_{(2, 60)} = 10.293$; $p < .001$; $\eta_p^2 = .255$]. Specifically, only in BI condition the difference between RTs in near (Mean = 356.088; SE

= 8.439) and far (Mean = 336.373; SE = 7.107) positions resulted significant (Mean difference = 19.715; SE = 3.945; p < .001) (figure 4).

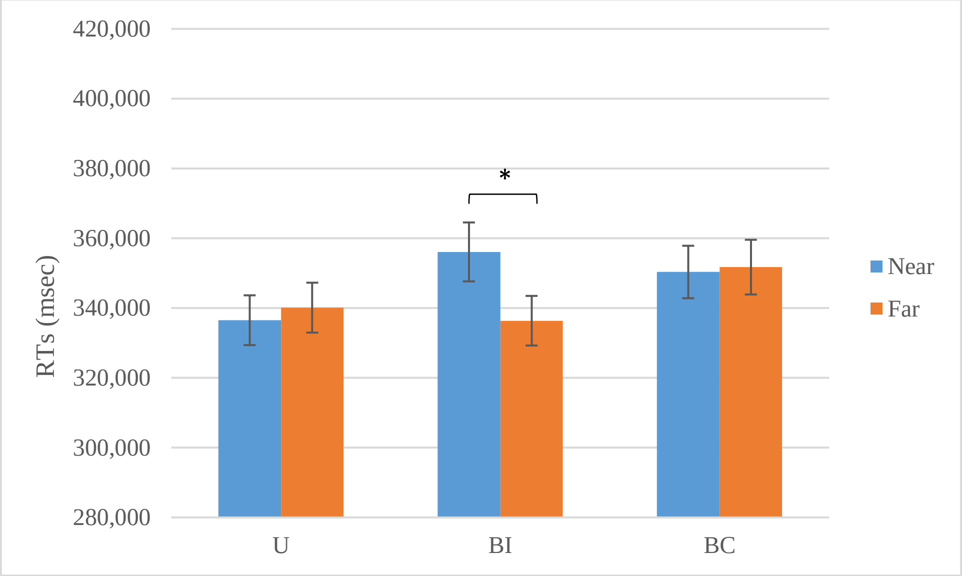


Figure 4. *Interaction between Condition and Position for the left hand. RTs in milliseconds are depicted for Unimanual (U), Bimanual Incongruent (BI) and Bimanual Congruent (BC) conditions. Blue bars represent the RTs in near position. Orange bars represent the RTs in far position. Black bars represent the standard error of the mean. Stars indicate a significant difference.*

Also the interactions between tDCS and Condition [$F_{(4, 120)} = 3.539$; p =.022; $\eta_p^2 = .106$] and between tDCS and Position [$F_{(4, 120)} = 4.665$; p =.013; $\eta_p^2 = .135$] resulted significant. Specifically, there was a significant difference between Sham and Anodic stimulation in BC condition (Mean difference = 24.367; SE = 6.283; p = .002). In other words, the Anodic stimulation reduced the RTs in BC condition (Mean = 340.530; SE = 7.598) compared to RTs of the same condition during Sham stimulation (Mean = 364.896; SE = 8.100). Furthermore, the difference between Sham and Anodic stimulation was significant in the near position (Mean difference = 2.504; SE = 8.173; p = .040). Indeed, the RTs for near position were faster in Anodic (Mean = 338.930; SE = 8.005) than Sham stimulation (Mean = 360.434; SE = 7.959). Lastly, the three-way interaction between tDCS, Condition and Position resulted significant [$F_{(4, 120)} = 4.219$; p =.007; $\eta_p^2 = .123$].

Because of the three-way interaction, three different repeated measure ANOVA were conducted for each condition (U, BC, BI) considering tDCS and Position as within subjects factors. The between subjects factor Group was excluded by the analysis because neither main effect not interactions were found.

In the U condition, neither main effects nor interactions were found.

In the BI condition, only a main effect of Position resulted significant [$F_{(1, 31)} = 23.208$; $p < .001$; $\eta_p^2 = .428$]. Specifically, RTs in far position (Mean = 337.047; SE = 7.240) resulted shorter than RTs in near position (Mean = 356.392; SE = 8.332).

In the BC condition, there was a main effect of tDCS [$F_{(2, 62)} = 6.823$; $p = .002$; $\eta_p^2 = .180$] and a significant interaction between tDCS and Position [$F_{(2, 62)} = 8.045$; $p = .001$; $\eta_p^2 = .206$]. Specifically, there was a general reduction of RTs in Anodic (Mean = 341.364; SE = 7.834) compared to Sham stimulation (Mean = 365.645; SE = 8.237). Furthermore, only in near position, the difference between Sham (Mean = 375.864; SE = 10.331) and both Anodic (Mean = 336.201; SE = 8.041) and Cathodic (Mean = 340.851; SE = 9.013) stimulations resulted significant (Anodic: mean difference = 39.663; SE = 9.488; p = .001, Cathodic: mean difference = 35.013; SE = 10.552; p = 007) (figure 5).

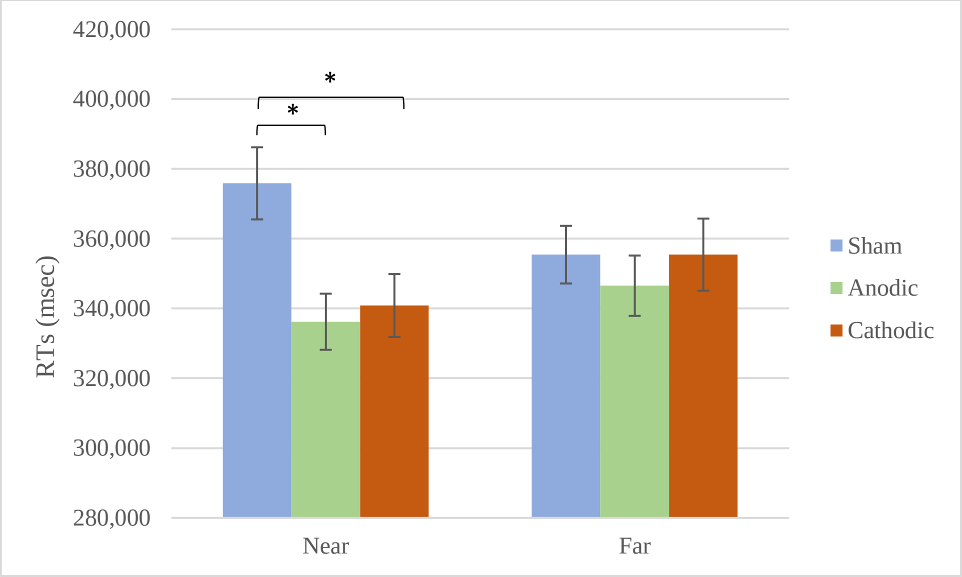


Figure 5. *Interaction between tDCS and Position for the right hand in Bimanual Congruent Condition. RTs in milliseconds are depicted for near and far positions in each kind of stimulation. Blue bars represent Sham stimulation. Green bars represent Anodic stimulation. Red bars represent Cathodic stimulation. Black bars represent the standard error of the mean. Stars indicate a significant difference.*

4.4 Movement Times

Right hand

On right hand a main effect of Condition was found [$F_{(2,\ 60)} = 157.955$; $p < .001$; $\eta_p^2 = .840$]. Specifically, U condition differed from both BI (Mean difference = 70.618; SE = 4.560; $p < .001$) and BC (Mean difference = 33.177; SE = 3.805; $p < .001$) conditions. Furthermore, BC condition differed from BI condition (Mean difference = 37.441; SE = 3.484; $p < .001$). MTs were shorter in U condition (Mean = 246.079; SE = 9.478) than both BC (Mean = 279.256; SE = 10.611) and BI (Mean = 316.697; SE = 11.465) conditions. Furthermore, the MTs in BC condition were shorter than MTs in BI condition. Also the main effect of Position was significant [$F_{(1,\ 30)} = 487.903$; $p <.001$; $\eta_p^2 = .942$] driven by shorter MTs in near (Mean = 232.002; SE = 9.838) than far position (Mean = 329.352;

SE = 11.179). Neither main effect of tDCS [$F_{(2, 60)} = .669$; $p = .516$; $\eta_p^2 = .022$] nor main effect of Group [$F_{(1, 30)} = .072$; $p = .790$; $\eta_p^2 = .002$] were significant.

A significant interaction between Condition and Position was found [$F_{(2, 60)} = 170.255$; $p <.001$; $\eta_p^2 = .850$]. Specifically, the difference between near and far position in BI condition (Mean difference = 12.056; SE = 5.344; p = .032) was significantly reduced compared to the same difference in both U (Mean difference = 138.005; SE = 6.948; p < .001; $t_{(31)} = 13.902$; p < .001) and BC (Mean difference = 141.990; SE = 6.751; p < .001; $t_{(31)} = 16.931$; p < .001) conditions. No difference were found comparing the near-far difference between U and BC conditions ($t_{(31)} = .775$; p = .444) (figure 6).

Lastly, the three-way interaction between tDCS, Condition and Group resulted significant [$F_{(4, 120)} = 2.531$; $p =.044$; $\eta_p^2 = .078$]. For this reason, two different repeated measures ANOVA were conducted for each group separately (P4 and P3) considering tDCS, Condition and Position as within subjects factors.

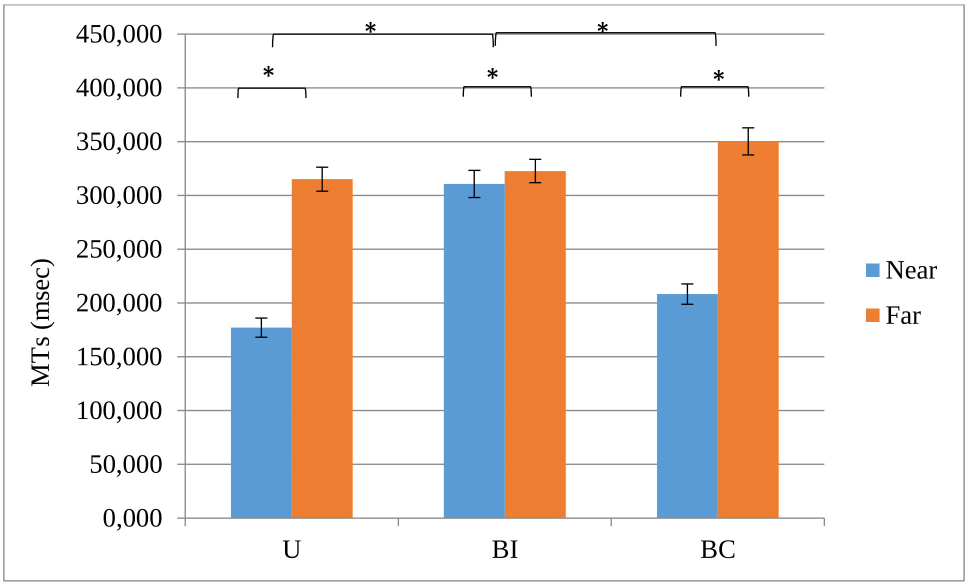


Figure 6. *Interaction between Condition and Position for the right hand. MTs in milliseconds are depicted for Unimanual (U), Bimanual Incongruent (BI) and Bimanual Congruent (BC) conditions. Blue bars represent the MTs in near position. Red bars represent the MTs in far position. Black bars represent the standard error of the mean. Stars indicate a significant difference.*

P4

On right hand we found a main effect of Condition [$F_{(2, 64)} = 87.755$; $p < .001$; $\eta_p^2 = .843$]. Specifically, there was a difference between U and both BC (Mean difference = 36.358; SE = 5.395; $p < .001$) and BI (Mean difference = 72.808; SE = 5.983; $p < .001$) conditions, furthermore a difference was found between BC and BI condition (Mean difference = 36.449; SE = 5.275; p = <.001) . Indeed, participants showed shorter MTs in the U condition (Mean = 247.052; SD = 13.358) than both BC (Mean = 283.410; SD = 16.239) and BI (Mean = 319.859; SD = 15.628) conditions. Furthermore, MTs were shorter in BC than BI condition. We also found a main effect of Position [$F_{(1, 16)} = 245.549$; $p < .001$; $\eta_p^2 = .939$] with shorter MTs in near (Mean = 236.549; SD = 14.312) than in far position (Mean = 330.332; SD = 15.813). No main effect of tDCS was found [$F_{(2, 32)} = .975$; $p = .388$; $\eta_p^2 = .057$].

We found an interaction between Condition and Position [$F_{(2, 32)} = 66.933$; $p < .001$; $\eta_p^2 = .807$] driven by a difference between near and far position in both U (Mean difference = 127.037; SE = 9.584; $p <.001$) and BC (Mean difference = 139.493; SE = 8.984; $p <.001$) conditions but not in the BI condition (Mean difference = 14.818; SE = 8.706; $p = .108$). Neither interaction between tDCS and Condition [$F_{(4, 64)} = .912$; $p = .462$; $\eta_p^2 = .054$], nor between tDCS and Position [$F_{(2, 32)} = .551$; $p = .582$; $\eta_p^2 = .033$], nor between tDCS, Condition and Position [$F_{(4, 64)} = 1.859$; $p = .129$; $\eta_p^2 = .104$] were found.

P3

On right hand we found a main effect of Condition [$F_{(2, 28)} = 73.680$; $p < .001$; $\eta_p^2 = .840$]. Specifically, there was a difference between U and both BC (Mean difference = 29.996; SE = 5.314; $p < .001$) and BI (Mean difference = 68.428; SE = 6.951; $p < .001$) conditions, furthermore a difference was found between BC and BI condition (Mean difference = 38.432; SE = 4.387; p = <.001). Indeed, participants showed shorter MTs in the U condition (Mean = 245.106; SD = 13.339) than both BC (Mean = 275.102; SD = 13.083) and BI (Mean = 313.534; SD = 16.798) conditions. Furthermore, MTs were shorter in BC than BI condition. We also found a main effect of Position [$F_{(1, 14)} = 242.165$; $p < .001$; $\eta_p^2 = .945$] driven by shorter MTs in near (Mean = 227.455; SD = 13.245) than far (Mean = 328.373; SD = 15.658) position (Mean difference = 100.918; SE = 6.485; $p < .001$). No main effect of tDCS was found [$F_{(2, 28)} = .094$; $p = .910$; $\eta_p^2 = .007$].

We also found an interaction between Condition and Position [$F_{(2, 28)} = 115.004$; $p < .001$; $\eta_p^2 = .891$], driven by a difference between near and far position in both U (Mean difference = 148.974; SE = 10.042; $p <.001$) and BC (Mean difference = 144.486; SE = 10.149; $p <.001$) conditions but not in the BI condition (Mean difference = 9.293; SE = 5.648; $p = .122$). Also the interaction between tDCS and Condition was significant [$F_{(4, 56)} = 3.414$; $p = .014$; $\eta_p^2 = .196$]. Specifically, the difference between U and BC condition was significantly reduced ($t_{(14)} = 2.870$; $p = .012$) by cathodic stimulation (Mean difference = 26.507; SE = 5.167; $p < .001$) compared to the same difference in sham stimulation (Mean difference = 36.509; SE = 7.610; $p = .001$). Furthermore, the interaction showed an increased difference between U and BI condition ($t_{(14)} = -3.057$; $p = .009$) in cathodic (mean difference = 80.823; SE = 8.727; $p <.001$) than anodic stimulation (mean difference = 57.776; SE = 7.904; $p < .001$). Lastly, the interaction highlighted a higher difference ($t_{(14)} = -2.959$; $p = .010$) between BC and BI condition in cathodic (mean difference = 54.316; SE = 5.877; $p <.001$) than anodic stimulation (mean difference = 30.805; SE = 5.266; $p <.001$) (figure 7). Neither interaction between tDCS and Position [$F_{(2, 28)} = 1.350$; $p = .276$; $\eta_p^2 = .088$] nor between tDCS, Condition and Position [$F_{(4, 56)} = .546$; $p = .565$; $\eta_p^2 = .038$] were found.

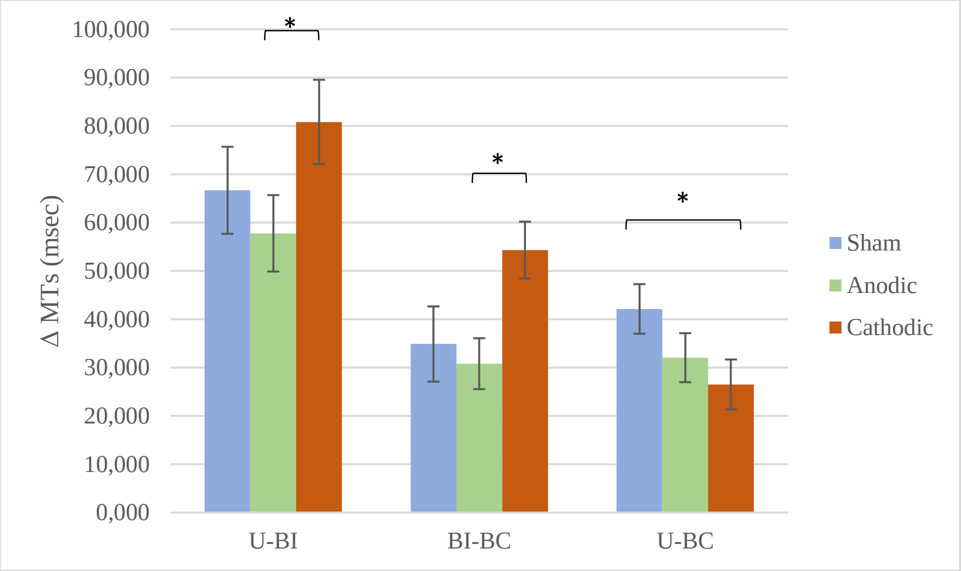


Figure 7. *Interaction between tDCS and Condition for the right hand in P3. Differences between Movement Times (Δ MTs) of the three conditions are depicted for each type of stimulation. Blue bars represent the difference between conditions in Sham stimulation. Green bars represent the difference between conditions in Anodic stimulation. Red bars represent the difference between conditions in Cathodic stimulation. Black bars represent the standard error of the mean. Stars indicate a significant difference. U-BI: difference between Unimanual and Bimanual Incongruent conditions; BI-BC: difference between Bimanual Incongruent and Bimanual Congruent conditions; U-BC: difference between Unimanual and Bimanual Congruent conditions.*

Left Hand

On left hand a main effect of Condition was found [$F_{(2,\ 60)} = 131.793$; $p < .001$; $\eta_p^2 = .815$]. Specifically, U condition differed from both BI (Mean difference = 69.356; SE = 5.007; $p < .001$) and BC (Mean difference = 32.925; SE = 4.402; $p < .001$) conditions. Furthermore, BC condition differed from BI condition (Mean difference = 36.431; SE = 3.217; $p < .001$). MTs were shorter in U condition (Mean = 255.303; SE = 8.779) than both BC (Mean = 288.228; SE = 11.324) and BI (Mean = 324.659; SE = 12.155) conditions. Furthermore, the MTs BC condition were shorter than MTs of BI condition. Also the main effect of Position was significant [$F_{(1,\ 30)} = 563.499$; $p <.001$; $\eta_p^2 = .949$] driven by shorter MTs in near (Mean = 239.452; SE = 9.560) than far position (Mean = 339.341; SE

= 11.860). Neither main effect of tDCS [$F_{(2, 60)} = 1.183$; $p = .314$; $\eta_p^2 = .038$] nor of Group [$F_{(1, 30)} = .022$; $p = .884$; $\eta_p^2 = .001$] were found.

Furthermore, only the interaction between Condition and Position resulted significant [$F_{(2, 60)} = 165.275$; $p < .001$; $\eta_p^2 = .846$]. Specifically, the interaction was driven by a reduced difference between near and far position in BI condition (Mean difference = 27.096; SE = 4.534; $p < .001$) compared to the same difference in both U (Mean difference = 131.083; SE = 5.344; $p < .001$; $t_{(31)} = 9.810$; p <. 001) and BC conditions (Mean difference = 141.488; SE = 7.240; $p < .001$; $t_{(31)} = 11.267$; $p < .001$). The same comparison between U and BC did not resulted significant ($t_{(31)} = -1.140$; $p = .263$) (Figure 8).

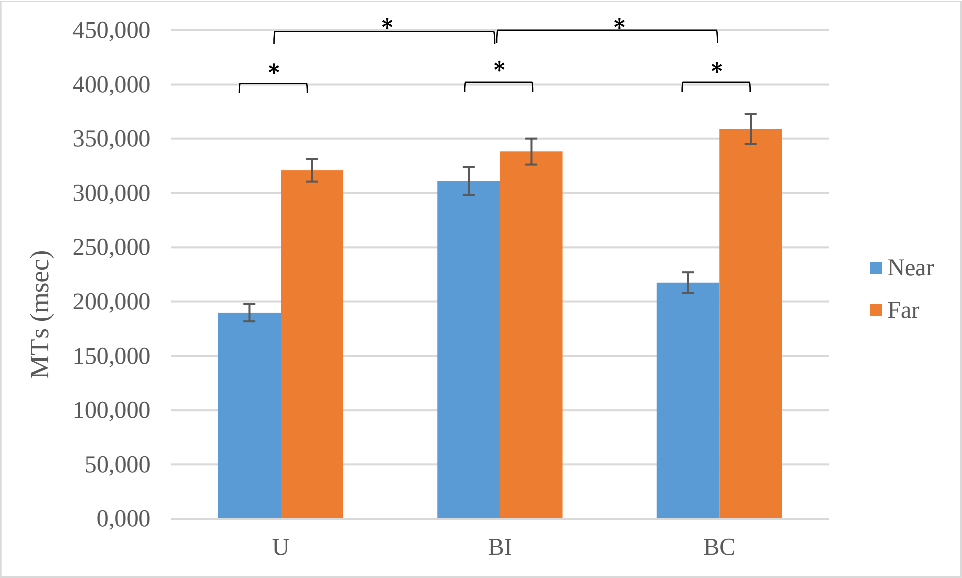


Figure 8. *Interaction between Condition and Position for the left hand. MTs are depicted for Unimanual (U), Bimanual Incongruent (BI) and Bimanual Congruent (BC) conditions. Blue bars represent the MTs in near position. Red bars represent the MTs in far position. Black bars represent the standard error of the mean. Stars indicate a significant difference.*

4.5 Inter Response Interval

All IRIs resulted significantly different from zero for both BC and BI conditions at the start and at the end of each movements in each different type of stimulation ($p < .001$) (figure 9).

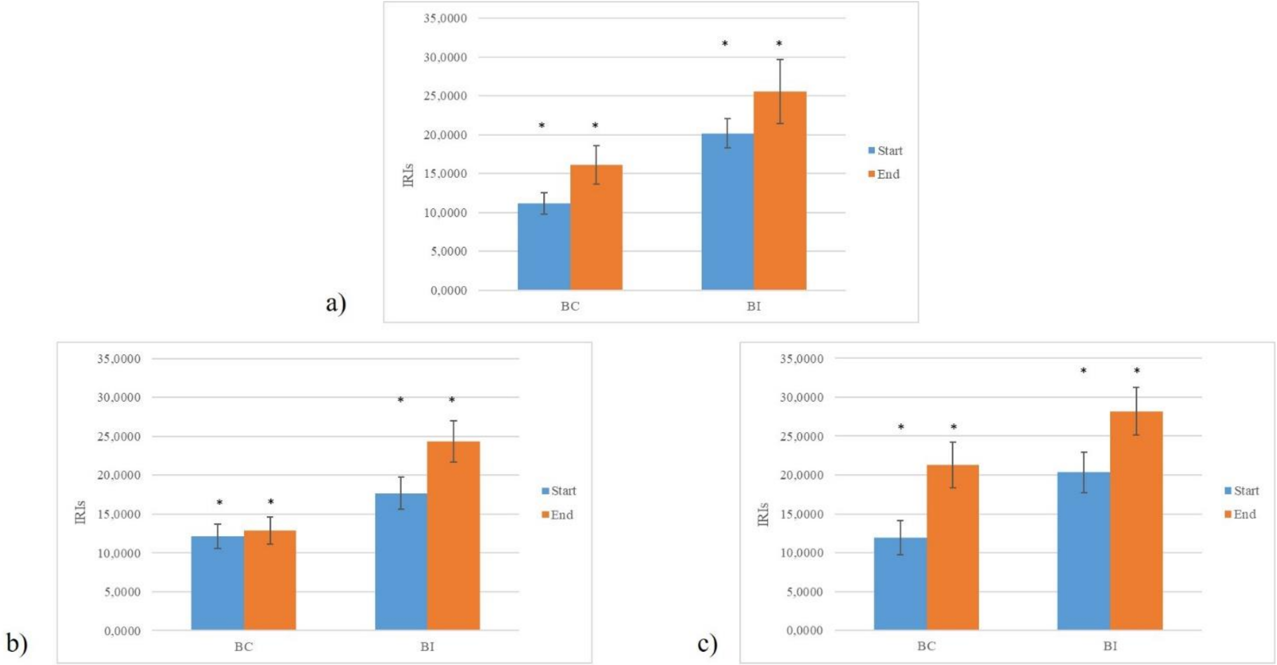


Figure 9. *Difference of Inter Response Intervals (IRIs) from 0 in each kind of stimulation (a: Sham; b: Anodic; c: Cathodic). Blue bars represent IRIs at the start of the movement. Orange bars represent IRIs at the end of the movement. Black bars represent the standard error of the mean. Stars represent a significant difference from 0.*

After the repeated measures ANOVA, a main effect of tDCS was found [$F_{(2, 60)} = 4.593$; $p = .022$; $\eta_p^2 = .133$] driven by a significant difference between Anodic and Cathodic stimulation (Mean difference = 4.788; SE = 1.700; $p = .026$). Specifically, the IRI was larger in Cathodic (Mean = 22.805; SE = 2.021) than Anodic stimulation (Mean = 18.017; SE = 1.179). Also a main effect of Condition resulted significant [$F_{(1, 30)} = 46.938$; $p < .001$; $\eta_p^2 = .610$] driven by larger IRI in BI (Mean = 25.205; SE = 1.525) than BC condition (Mean = 15.061; SE = 1.261). Furthermore, the main effect of Location resulted significant as well [$F_{(1, 30)} = 12.516$; $p = .001$; $\eta_p^2 = .294$] with larger IRI at the End of each movement (Mean = 22.597; SE = 1.714) compared to the IRI at the Start of each movement (Mean = 17.568; SE = .957).

The interaction between Location and Group was significant [$F_{(1, 30)} = 5.046$; p = .032; $\eta_p^2 = .044$]. Specifically, the group with the stimulation over P4 showed shorter IRI (Mean = 15.577; SE = 1.310) compared with the group with the stimulation over P3 (Mean = 19.560; SE = 1.395) only at the Start of the movement (Mean difference = 3.983; SE = 1.914; p = .046). Also the interaction between tDCS and Location resulted significant [$F_{(2, 60)} = 16.058$; $p < .001$; $\eta_p^2 = .349$]. This interaction showed that, only at the end of the movements, the Cathodic stimulation increased the IRI (Mean = 28.567; SE = 3.049) compared to both Anodic (Mean = 18.791; SE = 1.610; p = .002) and Sham (Mean = 20.434; SE = 1.514; p = .021) stimulations (Figure 10).

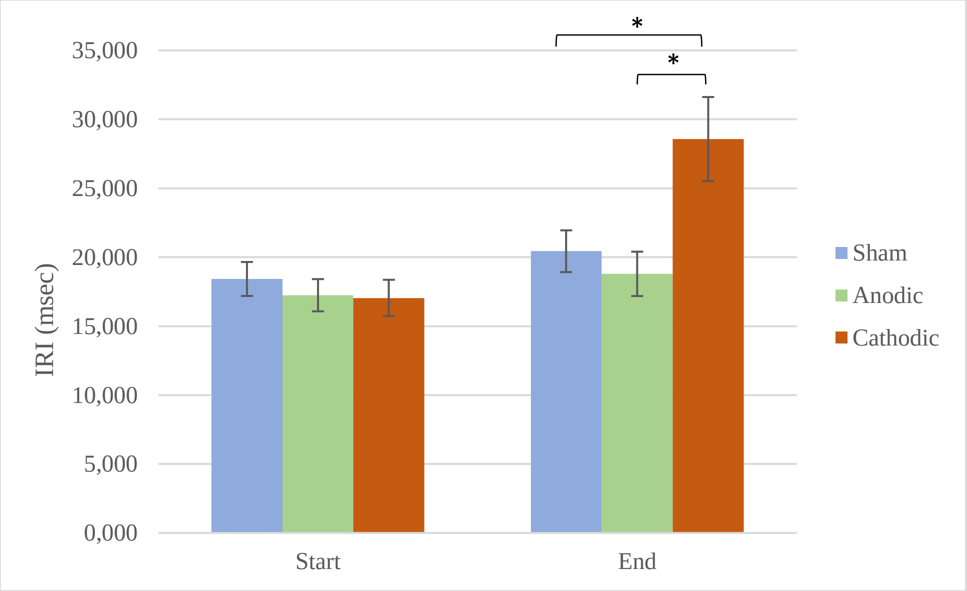


Figure 10. *Interaction between tDCS and Location. Inter Response Intervals (IRIs) are depicted in milliseconds (msec) at the Start and at the End of the movement. Blue bars represent IRIs for Sham stimulation. Green bars represent the IRIs for Anodic stimulation. Red bars represent IRIs for Cathodic stimulation. Black bars represent the standard error of the mean. Stars indicate a significant difference.*

5. Discussion

When different movements are performed with the two hands at the same time, an interference between the hands may arise (Bozzacchi et al., 2017). The bimanual temporal coupling is an example of such interference: the hands, moving towards targets differently located in the space, tend to synchronize their velocity in order to reach targets at the same time (Kelso, Southard, & Goodman, 1979a, 1979b). Evidence support the pivotal role of parietal areas being responsible for the interference of one hand on the other in eliciting the so-called bimanual coordination (Ullén et al., 2003; Wenderoth et al., 2005). Less explored, it is the different contribution of each hemisphere in determine the temporal coupling effect. Some studies described a dominance of the right hemisphere in the bimanual coupling effect (Diedrichsen et al., 2005; Garbarini et al., 2014; van den Berg et al., 2010; N. Wenderoth et al., 2004), whilst a dominance of the left hemisphere in bimanual movements has been hypothesized in right-handers (Stucchi & Viviani, 1993; Walsh et al., 2008). Conversely, another study attested an absence of hemispheric dominance in the bimanual coupling (Bozzacchi et al., 2017). However, different paradigms were used and the focus was not always on the bimanual temporal coupling effect.

The aim of the present study was to explore the role of the right and left parietal areas in the bimanual temporal coupling effect. For this reason, we administered 32 healthy participants with three different kind of tDCS (Sham, Anodic and Cathodic) in order to interfere with the activity over the left and the right parietal area respectively, during the same bimanual coordination paradigm used in the seminal work of Kelso et al. (1979). For this reason, participants were divided randomly into two different groups depending on which areas they received the stimulation.

Our results highlight different findings: (i) the temporal coupling is an illusory effect led by differences at the start of the movement; (ii) the hands are not synchronized neither at the start nor at the end of bimanual movements; (iii) tDCS does not affect the temporal coupling effect; (iv) there is not a clear lateralisation of bimanual movements.

Temporal coupling as illusory effect

The first result is partially in line with studies adopting similar paradigms (Kelso et al., 1979b; Pia et al., 2013; Shea et al., 2012). Accordingly with the Fitt's law (Fitts & Peterson ', 1964), a hand moving alone takes more time to reach the far target than the near one. Indeed, in this study during the Unimanual (U) condition both hands took more time to reach the far target. This difference remained the same during the Bimanual Congruent (BC) condition (when the two hands were moving towards targets similarly located in the space) but it was reduced during Bimanual Incongruent (BI) condition. In this case, the same hand took similar time to reach the target regardless its location (near or far). This result has been interpreted by previous studies as bimanual temporal coupling effect where the two hands modify their velocity to reach differently located targets at the same time (Bozzacchi et al., 2017; Kelso et al., 1979a, 1979b; Pia et al., 2013). Specifically, when a hand is moving towards the near target, it reduces its velocity in order to synchronise with the hand moving towards the far target (Corcos, 1984; Kelso et al., 1979b). However, our results on RTs attested how this effect was led by the different velocity already at the start of the movement. Previous studies do not take in to account RTs (Shea et al., 2012) or they do not detect any difference on this parameter, attributing the temporal coupling effect to the slow velocity of the hand reaching the near target (Kelso et al., 1979b; Pia et al., 2013). Conversely, present results attested how a hand starts later when it is moving towards the near target compared with its starting time when aimed at the far target. Bozzacchi et al. (2017) found similar results showing slower RTs for near than far targets in both bimanual congruent and incongruent movements. In other words, even when the two hands are aimed at different located targets, the hand moving towards the nearest one started after the other hand. It would be possible that the two hands do not act as a single unit, differently from what Kelso et al. (1979) stated. On the contrary, the timing for each hand would be decided in a separate manner, although the timing of the other hand is taken into consideration. In other words, motor programs for the two hands interact and this interaction is manifested already at the start of the movement. In summary, it seems that the bimanual temporal coupling is only an illusory effect since hands have different velocity at the start of the movement and this seems to be the cause underlying the temporal coupling effect.

Hands synchronization

Present results showed an absence of hands' synchronization also at end of each bimanual movement. If it is true that the hand reaching the near target slowed during the incongruent movement, this does not mean that the hands were perfectly synchronize at the end of the movement. Indeed, the disparity between hands resulted significantly different from zero in all the bimanual conditions both at the start and at the end of the movements. However, differently from other works, the hands were not directly compared here. Differences in these results could be related to a methodological issue, although others report an absence of synchrony during bimanual movements as well (Corcos, 1984; Fowler, Duck, Mosher, & Mathieson, 1991; Marteniuk et al., 1984). Specifically, Marteniuk et al. (1984) reported temporal asynchrony during bimanual movements in both RTs and MTs. As these authors noted, also data in Kelso et al.' study (1979) showed such temporal asynchrony that was suppressed when total times (RTs + MTs) were considered. Furthermore, the authors removed all trials in which the disparity between hands was greater than 15msec (Kelso et al., 1979a). It would be possible that in most studies there is only an "illusory simultaneity". As stated above, it is more than plausible that two motor programs exist for right and left hand and that they are influenced by each other in addition to task requirements' influence (e.g. distance of targets) (Marteniuk et al., 1984).

tDCS modulation

As for the contribution of left and right parietal areas in temporal coupling effect, the stimulation did not modify the temporal coupling effect on MTs. The stimulation over left parietal area affected only the contralateral hand, whilst no effects of tDCS over right parietal area were found neither on the right nor on the left hand. Contrary to what hypothesized, the effect found refers to a general reduction of MTs in both U and BC conditions with an increase of MTs in BI condition in cathodic compared to the anodic stimulation. In other words, the effect of the cathodic stimulation on BI condition was the reverse compared to the same effect on U and BC conditions. As result, this effect changed the relation between all the conditions. What it is worth to highlight is that these results emerged in comparison to anodic stimulation and not to the baseline (sham). Probably, anodic and cathodic stimulation created some degree of interference in different directions on the motor program of the right hand and, for this reason, a difference between these two kinds of stimulation was apparent. Because the effect found on BI condition was the reverse to that on other conditions (increased MTs in BI condition, decreased MTs in U and BC conditions), it is possible to confirm that the mechanism related to bimanual incongruent movements is different to that involved in other types of movements. This is in accordance with all the studies demonstrating differences between unimanual, bimanual congruent and bimanual incongruent movements (Hughes and Franz, 2008; Obhi and Goodale, 2005; Ivry et al., 2004; Kelso et al., 1979).

Furthermore, looking at the results on U and BC conditions, the cathodic stimulation seems to create a greater interference than the anodic one but in the same direction, when compared to sham stimulation. When different type of interferences (inhibitory or excitatory) are introduced in a simple attentional and motor process (e.g. unimanual and bimanual congruent movements), the resulted output could be non-specific (e.g. general reduction of MTs) (Pirulli, Fertonani, & Miniussi, 2014). When, instead, different kind of interferences (inhibitory or excitatory) are introduced in a more complex system (e.g. bimanual incongruent movement), the result could be different between them (Pirulli et al., 2014). In this case, the inhibitory interference (cathodic stimulation) during the BI condition could represent an additional inhibitory mechanism to the interference played by the motor program of the other hand. It is as if the cathodic stimulation, disturbing the motor program of the right hand, had indirectly enhanced the weight of the left hand' motor program on the final motor output. This does not happen during the U and BC conditions because in these cases the system does not have any other interference mechanisms to manage. In support to this interpretation, evidence show how the cathodic stimulation can have different effects depending on several variables (Pirulli et al., 2014). Even if the inhibitory effect of the cathodic stimulation is well-established when applied on motor areas (Nitsche et al., 2008), other studies reported different results with an improving of performance during cathodic stimulation in visuo-motor coordination and time reproduction tasks (Antal et al., 2004; Moos, Vossel, Weidner, Sparing, & Fink, 2012; Vicario, Martino, & Koch, 2013). Furthermore, the cathodic stimulation seems to have different effects depending also on the degree of noise (additional neural activity) present in the system (Miniussi, Harris, & Ruzzoli, 2013). In the case of bimanual incongruent movements, it is assumed the presence of the inhibitory effect of the motor program of the other hand and so, it is present more noise in the system compared to unimanual and bimanual congruent movements. It is possible that the different results, founded on U and BC compared to BI condition, are related to the level of noise already present in the system. This explanation might be true only if the existence of two different motor programs interacting each other was postulated in bimanual incongruent movements (Marteniuk & MacKenzie, 1980; Marteniuk et al., 1984).

A similar explanation could in principle illustrate the results found on RTs. In this case, the effect of tDCS consisted in a reduction of RTs during both Anodic and Cathodic stimulation when a hand was starting the movement towards the near target in BC condition only. Also in this case, there was the same effect regardless the polarity of the stimulation (anodic or cathodic) and, also in this case, this same effect involved the simplest bimanual movement (congruent). Because no effect on RTs in BI condition was found, it is possible to confirm the different nature of these bimanual movements (Hughes and Franz, 2008; Obhi and Goodale, 2005; Ivry et al., 2004; Kelso et al., 1979). Incongruent movements require a more complex spatial representation compared to congruent movements that, conversely, demand attention only to one target to be performed (Diedrichsen et al., 2005). It is possible that the tDCS effect on RTs represents simply an attentional modulation on bimanual movements. It is well-known the involvement of parietal areas in the representation of the outcome and in the intention to act during bimanual movements (Grafton & Hamilton, 2007) as well as in visuo-spatial attentional processes (Corbetta et al., 1993). It is possible that, during the initiation of bimanual movements, the tDCS effect is detected only on attentional mechanism. As stated above, the mechanism underlying bimanual incongruent movements is more complex than that related to bimanual congruent ones and, for this reason, a quantifiable change after the stimulation is detected only on the simplest bimanual movement. In other words, the tDCS could not have enough power to interfere with a more complex mechanism during the initiation of the bimanual incongruent movement, even if its effect is detected on the final outcome, as attested by results on MTs. In both cases, however, the effect of the stimulation seems to be determined by the complexity of the process. Furthermore, the effect found on RTs is limited to targets in near position. The existence of a specific fronto-parietal network underlying the multisensory representation of peri-personal space, is attested in both humans (Gentile, Petkova, & Ehrsson, 2011; Makin, Holmes, Brozzoli, Rossetti, & Farnè, 2009) and monkeys (Avillac, Denève, Olivier, Pouget, & Duhamel, 2005; Graziano & Cooke, 2006). Our results are in line with other studies attested a difference in the motor behaviour depending on the distance (near or far) of the administered stimulus (Avenanti, Annela, & Serino, 2012; Graziano, Taylor, & Moore, 2002; Serino et al., 2009). Taken together, previous results showed a reduction of motor excitability when stimuli were presented near the hand compared with stimuli presented far away from the hand (Avenanti et al., 2012; Serino et al., 2009). The authors interpreted the result as a motor defensive behaviour, similar to what happens in presence of noxious stimuli (Farina et al., 2001). In our case, the tDCS' effect seems to facilitate the initiation of the movement when the stimulus was near. Probably, tDCS over parietal areas created interference in the above-mentioned mechanism resulting in faster RTs when a near visuo-spatial stimulus is presented. Regardless of the already discussed polarity of the stimulation, present results confirm how the parietal areas have also a pivotal role in the representation of the peri-personal space functional for motor behaviours.

Hemispheric dominance of bimanual movements

Because the above-mentioned tDCS' effects on MTs were evident only when the stimulation was over left parietal area, one could hypothesize a pivotal role of this area in determine bimanual movements. This conclusion would be in accordance with other studies on bimanual movements (Stucchi & Viviani, 1993; Walsh et al., 2008). However, the effect found on MTs refers to the right hand only, without any evidence on left hand. For this reason, it is not possible to conclude for a clear left-hemispheric dominance. Instead, one could argue a more likely susceptibility of the left parietal cortex to the modulation. Because the tDCS modulates the neural activity of brain areas already activated by tasks requirements (Wagner, Valero-Cabre, & Pascual-Leone, 2007), it is possible to hypothesize that left and right parietal cortex are different in activation degree, with the left one more activated because its dominance in right-handers (Stucchi & Viviani, 1993).

Conversely, data on RTs appear clearer in showing a bilateral hemispheric involvement in simple bimanual movements (congruent) with the predominance of the left parietal area in controlling the initiation of movement of both hands. Indeed, the effect following the right hemispheric stimulation was detected only on the contralateral hand, whilst the left hemispheric stimulation was manifested on both hands. These results are in line with fMRI studies attesting a left hemispheric activation asymmetry during reaching tasks (Chapman et al., 2002; Hinkley et al., 2009). As already discussed, the effect found on RTs is more likely related to attentional processes. In this scenario, it is possible that the left hemisphere is always implicated as main agent for attentional demand. A study shows that when participants perform symmetrical bimanual movements, they tend to manifest a visuo-spatial attentional bias directing the gaze always to the right hand (Buckingham & Carey, 2009). This kind of visuo-spatial bias towards the right side during bimanual movements could be related to a predominance of the left parietal areas during bimanual actions, as hypothesized by other studies (Stucchi & Viviani, 1993; Walsh et al., 2008).

In summary, even if data on RTs appear clearer in determining a left-right asymmetry in simple bimanual movements, future researches are needed in order to disentangle the role of attentional process from that of more complex processes like the intention to act or the complex representation of the motor output.

Chapter 4

Lateralization of body schema components

1.Introduction

Body Representation (BR) refers to the mental representation of our bodies, encompassing motor, sensory and semantic information (Holmes & Spence, 2004). Evidence supports the existence of different types of BR (de Vignemont, 2010): Body Image (BI) refers to the body lexical-semantic knowledge and Body Schema (BS) refers to a constant update of the representation during the movements performed to interact with the environment. Online BS updating occurs thanks to efference copy information and sensory feedback that allow to control the motor execution and to make predictions about one’s own body posture (Miall & Wolpert, 1996; Wolpert & Ghahramani, 2000).

As for neural underpinning of BR and in particular of the BS, evidence suggests a dominant role of the right hemisphere (Blanke, Ionta, Fornari, Mohr, & Maeder, 2010). A large body of evidence derives from studies on damaged patients with neglect (Coslett, 1998; de Vignemont, 2010; Schmidt et al., 2013; Vallar, Antonucci, Guariglia, & Pizzamiglio, 1993). However, neurophysiological studies on healthy individuals show heterogeneity respect to this evidence, identifying a bilateral anatomical basis of the BS (Kosslyn, Digirolamo, Thompson, & Alpert, 1998; Parsons et al., 1995; Zacks, Rypma, Gabrieli, Tversky, & Glover, 1999). For example, two event-related fMRI studies revealed a bilateral activation of the superior parietal cortex when individuals are required to update their upper limb postural representation (Parkinson, Condon, & Jackson, 2010; Pellijeff, Bonilha, Morgan, McKenzie, & Jackson, 2006). Furthermore, such an agreement on the role of the right hemisphere in BS is questioned by results that analyse in detail the relationship between tasks for BS and brain lateralisation (Schwoebel & Coslett, 2005).

Partially, this disagreement of evidence might be related to the complexity in identifying unambiguous tasks. Several studies (Ionta & Blanke, 2009; Ionta, Fourkas, Fiorio, & Aglioti, 2007; Schwoebel, Boronat, & Branch Coslett, 2002; Schwoebel & Coslett, 2005) adopt Motor Imagery (MI), the ability to mentally recall a motor act without any overt movement (Rumiati, Papeo, & Corradi-Dell'Acqua, 2010), to assess properties of the BS. This choice is based on the concept that efference copy information and feedback from sensory systems allow not only real action control and execution but also imaginative processes (de Vignemont, 2010). MI can be explored through explicit and implicit tasks (Jeannerod & Frak, 1999). In the explicit ones, like in the mental chronometry task, individuals actively use MI to solve the task (Decety, Jeannerod, & Prablanc, 1989; Schwoebel et al., 2002; Sirigu et al., 1996). Evidence from explicit tasks show a strong relationship between the time required to perform an action and that required to mentally simulate it (Collet, Guillot, Lebon, MacIntyre, & Moran, 2011; Decety et al., 1989). This has been attributed to the overlapping between processes involved in MI and those involved in real motor execution (Decety, 1996; Gerardin et al., 2000; Jeannerod, 2001; Jeannerod & Frak, 1999). The Hand Laterality Task (HLT) (Parsons, 1987) is a typical MI implicit task as individuals mentally rotate their own body part to match it with the presented stimulus when asked to judge the laterality of a body segment (Parsons, 1987). The biomechanical constraints (Parsons, 1987) make individuals slower and less accurate when the laterality judgement concerns a stimulus in a position that is difficult to reach with a real movement (awkward position) compared to a stimulus in a position that is easy to reach with a real movement (comfortable position). This effect is taken as a convincing proof that mental simulation of own body part movements occurs by means of a motor strategy during the performance (Parsons, 1987).

Despite similarities between tasks that involve MI (Osuagwu & Vuckovic, 2014), dissociations have been reported between implicit and explicit tasks with an association between left hemisphere lesions and impairments in both kinds of tasks (Schwoebel & Coslett, 2005). Interestingly enough, dissociations based on implicit versus explicit processing have been reported in other domains, in relation to cerebral lateralisation. For instance, facial expressions of emotions can be differently lateralised accordingly to the level of awareness required: emotional processing is mediated differently by the two hemispheres, with the right hemisphere being more involved in the unconscious and the left hemisphere in the conscious emotional processing (Gainotti, 2012; Sedda et al., 2013).

2. Aim

The aim of this study was to explore if brain lateralisation of the BS shows the same awareness dependants effects. In other words, if lateralization encompasses the entire BS components or if there is a different neural network underlying implicit and explicit components. Further, the aim of the experiment was to replicate the dissociation between imagery and laterality tasks in a sample of healthy individuals. This allows to avoid the influence of confounding variables such as a bilateral effect of the lesion (damages in one hemisphere can elicit abnormal activation in the controlesional hemisphere (Cramer et al., 2011; Krause & Cohen Kadosh, 2014), cognitive impairments and fatigue. To reach our aims, we used Transcranial Direct Current Stimulation (tDCS), a useful technique to interfere with brain activity in a controlled fashion. We administered implicit and explicit BS tasks recording Reaction Times (RTs) and accuracy for each task while participants underwent a cathodic stimulation of the right parietal area (P4; Brodmann Area 40), in order to affect BS processes. The null hypothesis is to observe differences between the baseline condition (sham tDCS) and cathodal stimulation in both tasks. This will confirm that the right hemisphere controls both implicit and explicit components of BS. Alternatively, if a difference is observed in only one task when the cathodal stimulation is applied, the conclusion will be in favour of a different hemispheric control for implicit and explicit components of the BS. Particularly, one could hypothesize that the right hemisphere might be controlling more implicit and automatic processes of BS.

3. Methods

3.1 Participants

The study enrolled 18 participants (Mean age ± SD: 25.27 ± 6.61; Mean school age ± SD: 14.5 ± 3.01; 14 M) from the student pool of Heriot-Watt University (Edinburgh, UK) in exchange for course credits.

All participants were right handed as measured by the Edinburgh Handedness Inventory short version (Veale, 2014) and without sensory, neurological or psychiatric impairments. A preliminary questionnaire controlled for the absence of these criteria.

Inclusion criteria for the administration of the tDCS were: absence of heart disease, absence of history of epilepsy, absence of metallic objects in the body, absence of history of migraine with aura phase, absence of drug treatment and, for the women, absence of pregnancy.

Informed consent was obtained prior participation in the experiment. The study was designed according to ethical standards of the Declaration of Helsinki and received approval from the ethical committee at Heriot-Watt University (approval number: 2016-160).

3.2 tDCS procedure

tDCS stimulation was delivered through a battery-driven constant current stimulator (TCT Research tDCS 1ch stimulator; 2012 TCT Research Limited, Hong Kong) using a pair of surface saline soaked sponge electrodes (5cm x 5cm) placed on the target areas. A cathodal stimulation was delivered in order to interfere with BS and a sham stimulation was adopted as control condition.

Cathodal stimulation intensity was set at 2 mA for 20 minutes with a ramp up and a ramp down periods of 20 seconds at the start and at the end of stimulation, complying with current safety guidelines (Fregni et al., 2015; Nitsche et al., 2008). During the sham stimulation the ramp up period lasted for 20 seconds followed by a ramp down period of 20 seconds. This ensured that the participants felt the initial itching sensation as if it were a true stimulation. Participants were always blind about the type of stimulation.

Areas of interest were identified using the international 10-20 system for EEG electrode placement (Jasper, 1958). A unilateral bipolar montage was used: the cathode was placed on P4 (Brodmann Area 40) and the reference electrode on the area above the ipsilateral eye.

All participants completed both tDCS conditions (Sham and Cathodal) over two different experimental sessions, separated by at least 1 day in order to avoid interference effects between the different stimulation types. Stimulation types order was counterbalanced and randomized between subjects.

3.3 Tasks

3.3.1 Laterality Quotient calculated through the Edinburgh Handedness Inventory

The Edinburgh Handedness Inventory Short Version (Veale, 2014) was adopted to ensure participants are right handed. The Laterality Quotient was calculated as the sum of the items score divided by the total number of the items (Veale, 2014). A cut off of 61 was used to enrol participants who have a right hand dominance (Veale, 2014).

3.3.2 Hand Laterality Task

The HLT requires to judge if a picture represents a left or a right hand (Parsons, 1987, 1994). We used a modified version of the HLT (Fiori et al., 2013, 2014). The pictures of the left back and palm hand were obtained by flipping the right pictures with Microsoft® Paint (Microsoft Corporation), to avoid morphological differences between the two hands that could work as a cue.

The right back/palm and the left back/palm pictures were presented in four different orientations: 0°; 90°; 180°; 270°. Comfortable postures were identified as 90° for the left hand and 270° for the right hand, while awkward postures as 270° for the left hand and 90° for the right hand (Fiori et al., 2013) (figure 1).

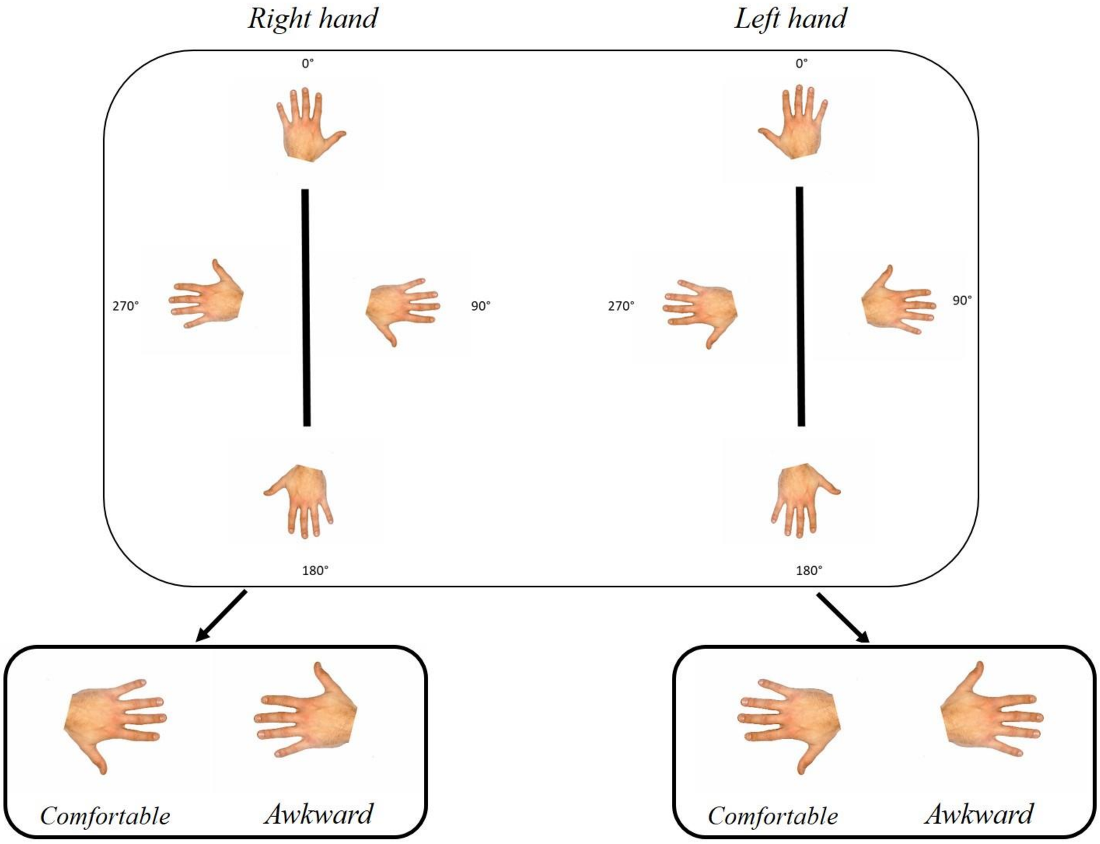


Figure 1. *Four different orientation for stimuli of both left and right hands are depicted in the upper part of the picture. Comfortable and awkward postures are depicted for both the left (on the left) and the right hand (on the right) in the lower part of the picture.*

The total number of stimuli was 16 (8 pictures of the right hand and 8 pictures of the left hand) in a back (4 for each hand) or palm (4 for each hand) perspective. The HLT was composed by a total of 96 trials divided in two blocks (48 trials for each block): every stimulus was presented 6 times (3 in the first and 3 in the second block) in a randomized order.

The pictures measured 1100 by 777 pixels, covering a vertical visual angle of 1.9° by 1.3° when the images were displayed at a distance of 50 cm. All the stimuli were presented on a computer screen

(13,3''; 16:9) with a resolution of 1920 x 1080 using Psycho-Py 1.83.03 (Psychology software in Pyton) (Peirce, 2007).

Participants seated in front of the pc screen (at the distance of 50cm) with their left and right index fingers on the “z” and “m” keys of the keyboard respectively. They had to answer as quickly and accurately as possible by pressing the “z” key if the picture on the screen is a left hand or by the “m” key if a picture is a right hand in one block and in the reverse way in the other block. The block order was randomized between participants. Every trial was preceded by a fixation cross lasting 1 second. The computer registered both RTs and the accuracy for every trial.

3.3.3 Mental Motor Chronometry

This task was modelled from the hand/imagery action task used in Sirigu et al., 1996. Movements selected for this task were: index and thumb opposition; thumb extension from the fist; middle finger crossed on the index finger; and extension of the index and the little fingers (Sirigu et al., 1996) (figure 2).

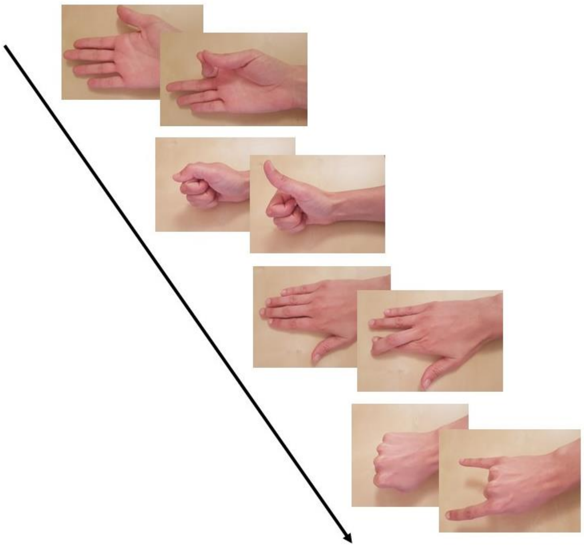


Figure 2. *Four movements in the Mental Motor Chronometry task (from the top: index and thumb opposition; thumb extension from the fist; middle finger crossed above the index finger; extension of the little and index fingers together). Only the right hand is depicted.*

The task was composed by two conditions. In the imagery condition, participants had to imagine each movement five times consecutively as quickly and as accurate as possible (Sirigu et al., 1996). In the real movement condition participants had to execute each movement 5 times as quickly and as accurately as possible (Sirigu et al., 1996). Participants were tested in both conditions with both hands. The order of the movements and the conditions was the same for every participant (from the index thumb opposition to the extension of the index and little fingers) starting with the imagery conditions (Schwoebel & Coslett, 2005; Sirigu et al., 1996) to avoid cognitive strategies, like counting (Sharma, Baron, & Rowe, 2009). The starting hand was counterbalanced and randomized between subjects. There were 8 trials in total in each condition because, differently from Sirigu et al. study (1996), we administered the task with both hands. Although in previous studies the movement time was recorded with a stopwatch (Schwoebel & Coslett, 2005; Sirigu et al., 1996), a computerized form of the task was adopted in order to collect more precise movement times.

Participants seated in front of the pc screen with their left or right index finger (depending of the starting hand) on the spacebar. After the instructions at the beginning of every trial, they had to close their eyes and to imagine or execute the target movement and, when finished, they pressed the spacebar immediately, open their eyes and passed to the next movement instructions (figure2).

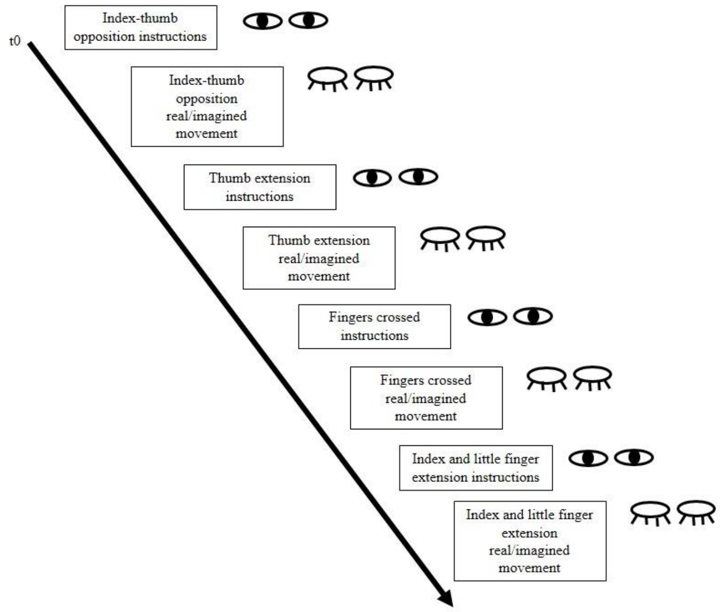


Figure 2. *Timeline of the Mental Motor Chronometry task (same structure is adopted for Real and Imagined conditions, the example shows the Imagine Condition only). Participants perform and imagine each movements with their eyes closed.*

3.4 Data analysis

Data were analysed with Statistical Package for Social Science (IBM® SPSS® Statistic, Version 22). We performed two different analysis separately for each task, as RTs in the HLT and movement times in the Mental Motor Chronometry (MMC) have a different magnitude (i.e. longer range for movement times than RTs).

Firstly, the presence of the typical effects reported in the literature (for the HLT the effect of biomechanical constraints and of stimulus orientation and for MMC the isochrony between real and imagined movements) (Decety et al., 1989; Parsons, 1987) was explored (preliminary analysis). The presence of these effects confirms the use of MI. After this step, we explored the effects of tDCS on BS and its components separately. Below a detailed explanation of these different analyses.

3.4.1 Hand Laterality Task Preliminary Analysis

RTs and accuracies were analysed. Firstly, data have been pre-processed for errors and outliers. RTs for trials in which the participants gave the wrong response were discarded from the analysis. Outliers were removed using a cut off of 2 standard deviations above and below the single participant mean (indicative of anticipation and lack of attention respectively) (Ratcliff & Roger, 1993).

After data pre-processing, RTs and accuracy means for every orientation (0°; 90°; 180°; 270°) and perspective (palm, back) for the left and right hand separately, both in the Sham and in the Cathodal stimulation condition, have been calculated.

Considering only the sham condition (no stimulation), data were analysed by means of paired sample t test (Bonferroni corrected) between 0° and 180° angles of rotation to estimate the effect of stimulus orientation and between comfortable and awkward postures to estimate the effect of biomechanical constraints (Fiori et al., 2013; Parsons et al., 1995). Alpha level was set at $p < .05$.

3.4.2 Mental Motor Chronometry Preliminary Analysis

For each participant, we first considered the average duration of each movement for the right and the left hand separately, both in the imagery and motor execution conditions, in Sham and Cathodal stimulation.

Outliers from movement times were removed separately in real and imagined conditions using a cut off of 2 standard deviations above and below the participant's mean, in order to discard the real and imagined inaccurate movements.

After data pre-processing, a correlation analysis using Pearson Coefficient was performed in order to check the temporal similarities between imagined and performed movements (isochrony).

3.4.3 tDCS effect on HLT

After confirming the effects of the HLT (stimulus orientation and biomechanical constraints), we explored the effects of the tDCS by means of two different repeated measure ANOVA with tDCS (Sham, Cathodic) and Postures (Awkward, Comfortable) or Orientation (0°, 180°) as within subjects' factors. We performed the same repeated measures ANOVA on both RTs and accuracies.

Alpha level was set at $p < .05$ for all analyses, post hoc comparisons were performed by means of estimates marginal means Bonferroni corrected. We report the effect size for significances as partial eta squared (ηp2) values.

3.4.4 tDCS effect on MMC

After confirming the presence of isochrony in the sham condition, the effects of stimulation were explored by means of a repeated measures ANOVA with tDCS (Sham, Cathodic) and Condition (Motor Imagery, Motor Execution) as within subjects' factors.

Alpha level was set at $p < .05$ for all analyses, post hoc comparisons were performed by means of estimates marginal means, Bonferroni corrected. The effect size for significances is reported as partial eta squared (ηp2) values.

4. Results

4.1 Preliminary analysis on HLT

In the HLT, we found a difference between RTs for awkward and comfortable postures ($t(17) = 2.717$; $p = .015$), with faster RTs in comfortable (Mean = 1813.52; ± SE = 199.55) compared to awkward (Mean = 2023.53; ± SE = 255.32) postures. We also found a difference between stimuli at 0° and 180° ($t(17) = -4.442$; $p < .001$), with faster RTs at 0° (Mean = 1675.76; ± SE = 149.36) compared to 180° (Mean = 2284.23; ± SE = 247.53) (Figure 3-a). For accuracies, we found only a significant difference between stimuli at 0° and 180° ($t(17) = 4.752$; $p < .001$), with higher accuracies for stimuli at 0° (Mean = 93.75; ± SE = 1.58) compared to accuracies at 180° (Mean = 80.09; ± SE = 3.11). No significant differences were found between accuracies in awkward and comfortable postures ($t(17) = -1$; $p = .331$) (Figure 3-b).

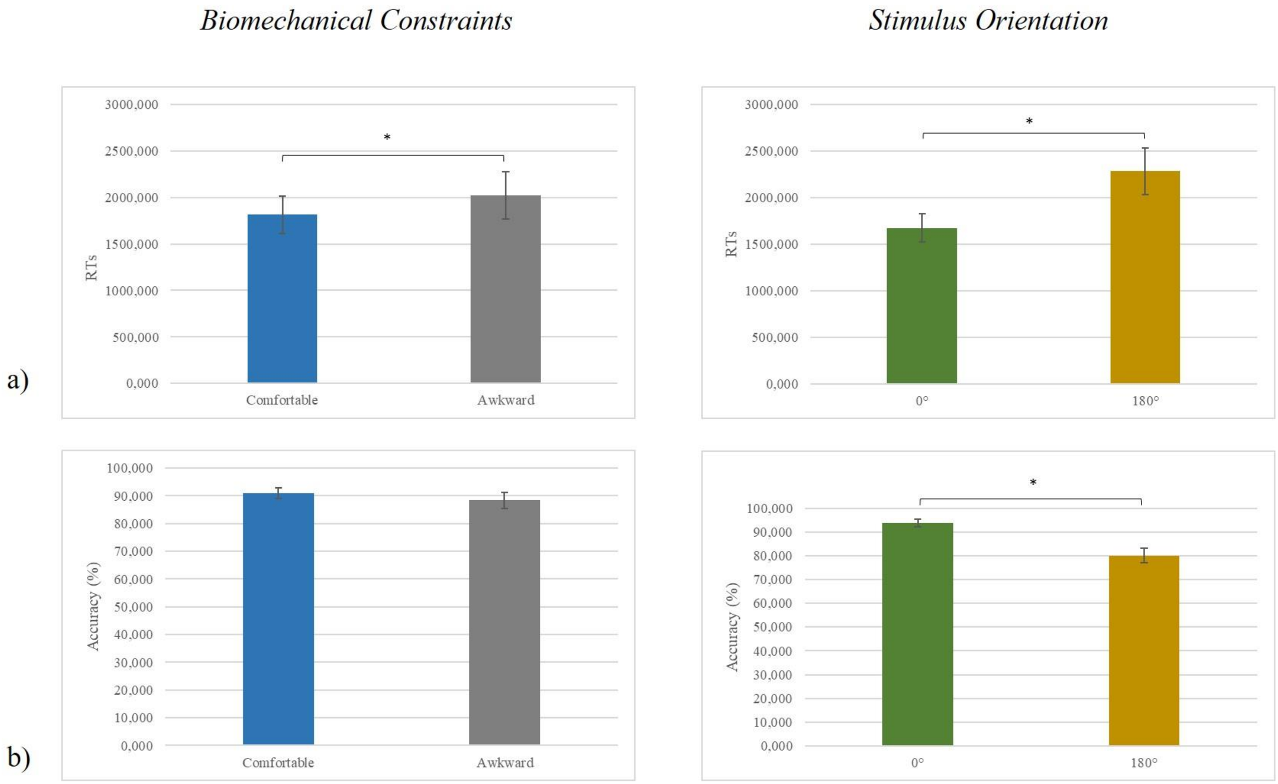


Figure 3. *Effect of biomechanical constraints (on the left) and of stimulus orientation (on the right) for both Reaction Times (RTs) (a) and Accuracy (b). Blue bars represent comfortable posture. Grey bars represent awkward posture. Green bars represent 0° oriented stimuli. Yellow bars represent 180° oriented stimuli. Numbers on the y-axis refer to RTs (a) and to Accuracy expressed in percentage (b). Stars represent a significant difference. Bars indicate the standard error of the mean.*

4.2 Preliminary analysis on MMC

Movement times for MI and ME in the MMC were positively correlated (r = .913; n = 18; p < .001).

4.3 tDCS effects on the HLT

We found a significant effect of Postures on both RTs [F(1, 17) = 8.966; p = .008; ηp2 = .345] and accuracies [F(1, 17) = 5.615; p = .030; ηp2 = .248]. RTs were faster in comfortable (Mean = 1745.24; ± SE = 151.66) than in awkward (Mean = 1956.30; ± SE = 208.84) postures. Similarly, accuracy was higher in comfortable (Mean = 91.31; ± SE = 2.00) than in awkward (Mean = 86.69; ± SE = 3.25) postures. Neither main effects of tDCS nor interactions between tDCS and Postures were found in both RTs (tDCS: [F(1, 17) = .936; p = .347; ηp2 = .052]; tDCS*Postures: [F(1, 17) = .001; p = .975; ηp2 = .000]) and accuracy (tDCS: [F(1, 17) = .433; p = .519; ηp2 = .025]; tDCS*Postures: [F(1, 17) = 1.821; p = .195; ηp2 = .097]).

We found a significant effect of Orientation on both RTs [F(1, 17) = 32.598; p < .001; ηp2 = .657] and accuracies [F(1, 17) = 17.330; p = .001; ηp2 = .505]. RTs were faster for stimuli at 0° (Mean = 1636.19; ± SE = 134.25) than at 180° (Mean = 2187.46; ± SE = 197.66). Accuracy was also higher at 0° (Mean = 92.24; ± SE = 1.88) than at 180° (Mean = 82.17; ± SE = 2.70). We did not find a main effect of tDCS in RTs [F(1, 17) = 1.205; p = .288; ηp2 = .066] nor in accuracies [F(1, 17) = .072; p = .792; ηp2 = .004]. We found a significant interaction of tDCS and Orientation in accuracies [F(1, 17) = 7.342; p = .015; ηp2 = .302] (figure 4) but not in RTs [F(1, 17) = .825; p = .376; ηp2 = .046]. The interaction found in accuracies was driven by a greater difference between stimuli at 0° and 180° during the Sham stimulation (Mean difference = 13.67; ± SE = 2.87; p < .001) compared to the Cathodal stimulation (Mean difference = 6.48; ± SE = 2.63; p = .025).

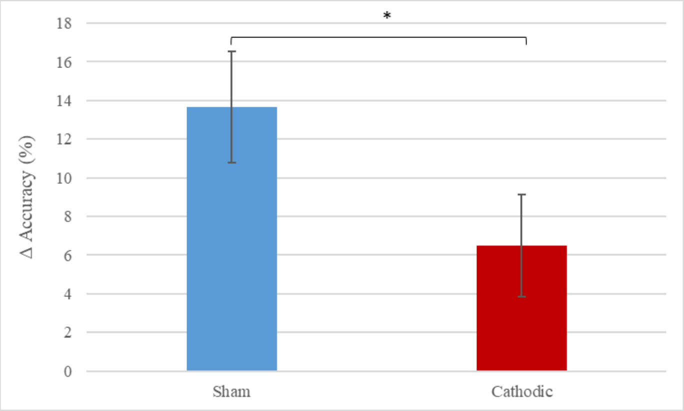


Figure 4. *Magnitude of the stimulus orientation effect in the Sham and Cathodic stimulation. Number on y-axis refer to Accuracy expressed in percentage. Blue bar represents the difference between 0° oriented and 180° oriented stimuli in sham stimulation. Red bar represents the difference between 0° and 180° oriented stimuli in cathodic stimulation. Star represents a significant difference. Bars indicate the standard error of the mean.*

4.4 tDCS effect on MMC

We found a significant effect of Condition [F(1, 17) = 6.561; p = .020; ηp2 = .278] with longer movement times in MI (Mean = 7031.64; ± SE = 545.08) than movement times in ME condition (Mean = 6330.15; ± SE = 520.71). Neither main effects of tDCS [F(1, 17) = .000; p = .987; ηp2 = .000] nor interactions of tDCS with Condition were found [F(1, 17) = .105; p = .750; ηp2 = .006].

5. Discussions

To interact with the environment, we need a lot of information, some of which are related to our Body Representation (BR). Specifically, our Body Schema (BS) is a constantly updated BR of the body parts in space, encompassing visual, motor, tactile and proprioceptive information (Holmes & Spence, 2004). Motor Imagery (MI) has been considered a good tool to explore BS proprieties, due to the temporal similarities between the time needed to imagine and the time needed to really perform movements (Collet et al., 2011; Decety et al., 1989). MI tasks used to explore BS show differences in requirements (Jeannerod & Frak, 1999). These tasks are classified in explicit (Decety et al., 1989) and implicit (Parsons, 1987) tasks, based on the awareness required to solve them. Performance dissociations between explicit and implicit tasks have been reported in patients with brain damage (Schwoebel & Coslett, 2005) depending on which component the task involves (Schwoebel & Coslett, 2005). Other evidence suggests that the BS might be lateralized to the right hemisphere (Blanke et al., 2010; Coslett, 1998).

To shed light on the lateralization of the BS and explore the role of tasks demands, we tested 18 participants during two different MI tasks (implicit and explicit) while cathodal or sham tDCS was delivered to the right parietal cortex (P4; Brodmann area 40). We recorded behavioural data (RTs and accuracy in the implicit task; movement times in the explicit task) in order to understand if interfering with a cathodal stimulation with the right parietal cortex processes modulates BS globally rather than selectively depending on awareness. After cathodal stimulation, we found a modulation in the implicit

MI task only. Specifically, the difference in accuracy between stimuli presented at 0° and at 180° was reduced compared to the baseline (sham) condition. No modulation was found in the explicit task.

In summary, our findings challenge the general notion that BS is controlled by the right hemisphere as a whole. One could hypothesize that implicit and explicit mechanisms are differently lateralised given that studies on other cognitive domains show how more automatic processes are related to the right hemisphere, while more explicit processes depend on the left one (Gainotti, 2012; Sedda et al., 2013). Furthermore, some neuroimaging studies show predominant activation in the left hemisphere during explicit MI tasks (Decety et al., 1994; Gerardin et al., 2000; Ingvar & Philipson, 1977). Similarly, some studies on left brain damaged patients show an impairment during explicit MI tasks (Schwoebel & Coslett, 2005; Sirigu et al., 1996; Sirigu & Duhamel, 2001).

Effects related to brain lateralization seems to be even more specific as in our implicit task, the Hand Laterality Task (HLT), tDCS selectively modulated the stimulus orientation effect and only in terms of performance accuracy. During cathodal stimulation of the parietal cortex, the difference between the error peak for most difficult stimuli (180° oriented) and the error peak for the easiest stimuli (0° oriented) was reduced. In detail, accuracy decreased for 0° oriented stimuli while increasing for 180° oriented stimuli. As such, even within a task, interference with brain body areas influences differently implicit MI processes. In order to explain these results, different scenarios can be taken into account.

One possibility is that during cathodal stimulation participants applied a visual instead of a motor strategy. This could explain why the stimulation influenced only the stimulus orientation effect and not biomechanical constraints processes. However, the presence of an effect of biomechanical constraints with longer RTs in awkward compared to comfortable postures in the baseline (sham) condition, attests that motor imagination occurred (Gentilucci, Daprati, & Gangitano, 1998), together with the mental rotation proved by the effect of the stimulus orientation (Jordan, Heinze, Lutz, Kanowski, & Jäncke, 2001).

Granted that our findings are unlikely to be related to different strategies adopted to solve the task, one has to consider that hands depicted at 0° and 180° orientation can also be processed basing on first- and third-person perspective respectively. First person perspective elicits a body ownership illusion (Maselli & Slater, 2013) so that faster RTs and higher accuracy for stimuli at 0° could be related to the so called "self-advantage" (Hoover & Harris, 2016). Conversely, slower RTs and poorer accuracy for 180° oriented stimuli could depend on the lack of self-advantage and not only on the 180° rotation of one's own hand. This makes intuitive why interfering with the right parietal lobe decreases the self-advantage, as right parietal areas modulate the sense of body ownership (Tsakiris, Costantini, & Haggard, 2008) and self-recognition (Feinberg & Keenan, 2005). Further, support to the right hemisphere being involved in self-body parts recognition derives from studies of Frassinetti and colleagues (Frassinetti, Maini, Romualdi, Galante, & Avanzi, 2008) on right brain damaged patients with poor performance at a visual matching-to-sample task only when the stimuli concerned their own body parts compared to those representing others' body parts. Another recent work adopting a similar task (Candini et al., 2016) shows a dissociation in brain damaged individuals as only right-brain damaged patients were impaired compared to left-brain damaged patients showing an intact performance.

Finally, if we take into account cognitive models specifically explaining the HLT, one might consider the theory by which this task requires two different processes in sequence to identify a hand as a right or left one (Gentilucci et al., 1998; Parsons, 1994). Accordingly to this theory, a first stage is the unconscious one in which the information about the hand laterality does not reach awareness, while the second stage is a conscious mental rotation-confirmation process. Our data did not disconfirm this hypothesis, but they challenge the idea that these processes are sequential because we found and effect only on the accuracies and not on RTs. It is plausible that the implicit analysis of the stimuli and the conscious mental confirmation process work in parallel. This point of view explains how a mental rotation can still take place even though the first step of the process is modulated. As the body and the functions related to it are so important, implicit tasks, like the HLT, might involve different processes with different levels of complexity working in parallel in order to guarantee as much as possible the maximum degree of efficiency even when one component is perturbed.

Summarizing, our data suggest that a white or black BS hemispheric lateralisation is not feasible due to the different weight given to the implicit and explicit components, both relevant to BS. Modulation of awareness requirement in tasks exploring the BS determines a different involvement of the two hemispheres, and consequently differences in evidence.

Chapter 5

General discussion and final remarks

The hemispheric lateralization has received attention across years because its implication in determine behavioural and individual differences (Ghirlanda & Vallortigara, 2004; Vallortigara & Rogers, 2005). Historically, the dominance of one hemisphere on the other has been proven by the study of brain damaged patients, allowing the identification of the left hemisphere as main agent for language functions (Broca, 1865) and the right one as main agent for visuo-spatial functioning (Newcombe and Ratcliff, 1989). In this scenario, the left hemisphere has been considered as the dominant one in human population and, for this reason, it receives a lot of attention regarding its specialization and its expansion in the course of the evolution with particular regard to the evolution of frontal areas (Sherwood et al., 2003; Spocter et al., 2010). Nevertheless, also the right hemisphere expanded in the course of the evolution (Aversi-ferreira et al., 2010). Specifically, the right parietal lobe increased its dimension and its connections, becoming a specialized area for the multisensory integration mechanisms (Kolb, & Whishaw, 2009). For these features, the parietal lobe has been defined as important as the brain areas for language functions, because it allows the interaction with the outside world (Iturria-Medina et al., 2011).

Taking into consideration the broad implication of both the right and the left parietal areas in different cognitive processes (Culham & Kanwisher, 2001), in this work three different stand-alone studies are proposed following a hierarchical structure from the most basic to the most complex cognitive mechanism. The first study explored the lateralization of the attentional mechanism in its perceptual and representational forms. The second study aimed at exploring the lateralization of the bimanual coordination in a visuo-spatial framework. Lastly, the third study explored the lateralization of a most complex domain, namely the Body Representation.

1.Summary of results

Visuo-spatial attention

Despite the growing evidence on the attentional mechanisms underlie visuo-spatial abilities, nowadays there are still unanswered questions, especially when taking into account a specific population: left-handers. Do the theories on attentional asymmetries apply also to the brain of left-handers? Further, is the parallel between the perceptual and representational domain still holding in this differently lateralized population?

To answer these questions, in the first study we compared the performance of right- and left-handers participants during two different tasks, assessing both representational and perceptual domains. As such, the present work represents the first direct comparison between right- and left-handers considering also the representational domain. Results show that representational and perceptual domains are differently affected by attentional biases more in left-handers than right-handers. In other words, attentional asymmetries affected in different way right- and left-handers depending on the domain (perceptual or representational). In summary, we show that the parallel between the perceptual and representational changes in this differently lateralized population, therefore theories on attentional asymmetries should be revised for left-handers.

Bimanual coordination

Because the visuo-spatial attentional mechanisms are useful in order to perform actions in the environment, in the second study it was explored the lateralization of a motor mechanism, namely the bimanual temporal coupling effect. This effect is manifested when the two hands perform different movements at the same time and coordinate themselves in a temporal manner.

To this aim, the transcranial Direct Current Stimulation (tDCS) was applied over both right and left parietal areas during a simple bimanual coordination task. The task was visuo-spatial in its nature because movements were cued by visuo-spatial stimuli. For this reason, it was hypothesized that the main agent, leading this effect, could be the right parietal area, even though there is a heterogeneity of results (van den Berg et al., 2010; Stucchi & Viviani, 1993; Walsh, Small, Chen, & Solodkin, 2008). Our findings demonstrate the complexity of this motor mechanism. Indeed, no evidence of the bimanual temporal coupling effect' lateralization was found. Furthermore, a left or right involvement of the parietal areas seems to depend on several variables (hand considered, complexity of the movement, distance of the stimulus from the own body). In summary, even if a clear lateralization of bimanual movements was not proved, we confirmed the involvement of the parietal areas in some fundamental features of the task (e.g. visuo-spatial attentional features and peri-personal space representation), although the global mechanism (bimanual temporal coupling) is more than the sum of its parts.

Body Representation

Visuo-spatial representations and motor information together, make the human beings capable to interact and perform actions in the environment properly. One of the most complex function subtending these fundamental functions is represented by the Body Representation (BR) and, more specifically, by the Body Schema (BS), a BR component involving several mechanisms (visuo-spatial, motor, tactile and proprioceptive information). Despite the growing evidence on BR deriving from both healthy individuals and brain damaged patients (Coslett, 1998; de Vignemont, 2010; Schmidt et al., 2013; Vallar, Antonucci, Guariglia, & Pizzamiglio, 1993), there is still heterogeneity in the lateralization of brain areas subtending this function. Some studies support a pivotal role of the right hemisphere (Blanke et al., 2010), others show a bilateral brain involvement (Kosslyn, Digirolamo, Thompson, & Alpert, 1998; Parsons et al., 1995; Zacks, Rypma, Gabrieli, Tversky, & Glover, 1999) and, finally, some report an association between the left hemisphere and impairments in BS (Schwoebel & Coslett, 2005). This heterogeneity makes it difficult to develop interventions and to fully understand BS as a cognitive function.

To determine if the BS is so clearly lateralized, we compared the performance of healthy participants during a sham and a cathodic tDCS delivered to the right parietal lobe while they performed two different BS related tasks. Importantly, the use of a non-invasive stimulation technique allowing to temporarily interfere with brain activity in a group of healthy participants, avoids confounding variables usually reported in studies on patients. Furthermore, we had the opportunity to administer different tasks tackling the BS, being able to consider task requirements in the general picture of BS lateralization. Our findings show that the inhibitory effect of the cathodic stimulation affects only one specific aspect of the BS. As such, our results challenge the general idea of a right hemispheric dominance, and rather suggest that conscious/unconscious processes of the BS rely on a bilateral network encompassing both the left and the right hemisphere.

2. General conclusion and future directions

Even if the three presented studies are independent, they aim at answering different questions concerning the common ground of the hemispheric lateralization. Although the studies are different, in all of them one element appears fundamental: the hemispheric lateralization of cognitive processes related to parietal areas seems to be totally dependent on the specific features considered. For instance, in the first study the considered domain (representational or perceptual) appears crucial in detecting differences between different lateralized populations. In the second study, the involvement of one hemisphere on the other emerged accordingly to the specific variable considered (e.g. task requirements, hand). Lastly, in the third study the level of awareness appears crucial in determining the main role played by the right hemisphere. In all of these presented studies, it appears clearly how a black or white lateralization is not feasible in relation to complex processes typically related to the parietal areas, because it always depends on the features of the task (e.g. domain, task requirements, awareness) and not on the cognitive process itself (e.g. visuo-spatial attention, bimanual coordination, BR). In a meta-analysis, Vogel et al. (2003) stated that considering different indices it is possible to produce different results and so, different interpretation of hemispheric lateralization (Vogel et al., 2003). It seems that when a cognitive process is explored, it must be considered carefully all the variables related to that process. This become fundamental for possible applications of the knowledge about hemispheric lateralization.

Whilst in the past the knowledge about the hemispheric lateralization was useful only in order to predict the outcome related to brain lesions (Broca, 1865), to date it appears fundamental to create specific interventions based on that outcome (Vogel et al., 2003). Indeed, in a clinical scenario it is not enough to know which cognitive process is impaired after a lateralized brain lesion to intervene properly on patients. On the contrary, the manipulation of specific variables could be crucial. This principle has been fully applied, for instance, in case of rehabilitation of neglect following right brain lesions. For example, it was proven that passive movements in the left hemispace can ameliorate the symptomatology only if those movements have a greater salience that movements simultaneously performed in the right hemispace (Frassinetti, Rossi, & Làdavas, 2001). This is only one example that proves how the study of specific variables and their manipulation related to a more general process can produce benefits in clinical practice.

Generally, studies on brain lateralization are aimed at answering to different questions (Prohovnik, 1978): (i) is the brain organization different in right- and left-handers? (ii) are right and left hemispheres differently organized? (iii) do right and left hemispheres elaborate contralateral stimuli only? In this thesis, different methodologies are used because each study complies with different questions. For these reasons, a further common discussion is not feasible.

However, in the second and in the third studies the same technique was used. In the study of hemispheric lateralization, it appears very important to explore which techniques can be used and for which purpose (Vogel et al., 2003). Nowadays, many techniques are applied to better account the brain organization. For instance, the electroencephalogram (EEG) and the functional Magnetic Resonance (fMRI) allow, in different way, to explore the lateralized brain activity during the execution of cognitive tasks or during rest (Bozzacchi et al., 2017; Si, Zhang, Zhang, & Jiang, 2017;

Strother, Zhou, Coros, & Vilis, 2017). Differently, neuromodulatory techniques, such as transcranial Direct Current Stimulation (tDCS) or Transcranial Magnetic Stimulation (TMS), allow to interfere with the normal brain activity. For this reason, they permit to make inferences about the lateralized areas related to a specific cognitive process (Brambilla, Manenti, Ferrari, & Cotelli, 2015; Duecker, Formisano, & Sack, 2013; Kwon, Kang, Lee, & Son, 2016; Passeri, Capotosto, & Di Matteo, 2015). However, the choice of which technique is better to use is not a simple point. Indeed, data collected with different techniques on the same cognitive process show different results and different conclusions about the hemispheric lateralization of the cognitive process could be drawn (Vogel et al., 2003). For instance, some studies involving fMRI attested a right lateralization for mental rotation processes (Cohen et al., 1996; Corballis, 1997) while, when the same process is investigated through the EEG no difference emerged between the two hemispheres (Milivojevic, Hamm, & Corballis, 2009). Such inconsistency of results does not clarify the issue of laterality and, instead, make it more confused (Vogel et al., 2003). When a study about lateralization is conducted with a specific technique, it is of fundamental importance to have clear the aim of the study, the features of the task and all the variables related to the considered cognitive process (Vogel et al., 2003). Here, we choose to use the tDCS because it is less focal than the TMS (Klooster et al., 2016). In the second study, the aim was to explore the contribution of the left and right parietal areas in a bimanual task while in the third study the aim was to explore the role of the right parietal area in different components of the BR. In both of the studies, the targeted areas were not so focal and, for this reason, the tDCS was preferable to another modulatory technique like the TMS. Whilst the latter allows to be more focal during the stimulation (targeting a specific area in order to interfere specifically with it), the tDCS appears a more suitable technique for our purposes given its more extensive area of control (Klooster et al., 2016). Even if the debate about the efficacy of the tDCS is out of matter here, it is worth to note that future studies are needed to fully understand the mechanisms related to this technique, also applying electric field modelling (Klooster et al., 2016). Specifically, when this technique is applied to complex processes, like mental imagery or complex motor behaviour, many variables could intervene in leading the direction of results (Bortoletto, Pellicciari, Rodella, & Miniussi, 2015; Fertonani & Miniussi, 2017). Furthermore, understanding which variables determined the tDCS effects, makes it possible to better understand how to apply the electric stimulation for rehabilitative purposes.

In summary, whilst at a first view the fragmentation of general cognitive processes appears counter-productive, it become fundamental when aimed to intervene in the clinical practice. The studies about lateralization could start to use a combination of different techniques together (e.g. tDCS and EEG, tDCS and fMRI, TMS and EEG and so on) to better account the brain organization. Furthermore, the inclusion of different lateralized population appears fundamental in this scenario clarifying how a different brain organization can affect the behavioural performance.

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